14.9.82
CUK-H-6211-9-P25824

July 198

THE BRITISH JOURNAL OF RADIOLOGY

(9)

X-ray diagnosis —
Radiation oncology
[illegible]
[illegible]
[illegible]
[illegible]
[illegible]
[illegible]

Published b
The British Institute of Radiolog

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

D. K. BEWLEY, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. HAYBITTLE, M.A., PH.D.,
A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

P, 25, 824

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01–935 6237 and 01–935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

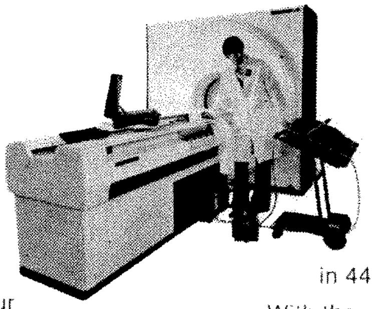
Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company has the largest CT service force in Europe?

General Electric Company of U.S.A:*
Proven support for proven systems.



General Electric of U.S.A. Medical Systems is the leader—not only in Europe but throughout the world—in computed tomography (CT) technology. And, matching this capability is our in-depth service force… helping to maintain optimum clinical performance.

Specifically, more than 350 engineers, technicians and support personnel service our full line of imaging systems from operations in 12 European countries. Each specialist is factory trained at the GE Medical Systems Institute and provided refresher courses to keep current with new products and technologies. Franchised distributors maintain service organisations in six additional countries. Parts are stocked in 44 depots throughout Europe.

With thousands of diagnostic imaging systems—CT, x-ray, nuclear and ultrasound—already operating across Europe, General Electric U.S.A. is committed to providing the service needed to keep them performing efficiently.

Service that protects your equipment investment. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

For more facts about diagnostic imaging equipment, visit the General Electric U.S.A., exhibit at the International Congress of Radiology in Brussels, June 24 - July 1, or telephone:

Frankfurt/M., Tel. 06 11/7 60 73 69 ● Wien, Tel. 24 14 51 ● Brussel, Tel. 660 2010 ● Kopenhagen, Tel.: 2 86 86 00 ● Mailand, Tel.. 753 1351 ● Breda, Tel.: 76 22 54 15 ● Lissabon, Tel. 36 71 55 ● Madrid Tel.. 252 5100 ● Goteborg, Tel.: 42 09 70 ● Zurich, Tel. 47 50 30

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

Knee Arthrography

D J Stoker, Director of Radiological Studies, Institute of Orthopaedics, Royal National Orthopaedic Hospital, London.

A practical account of the use of arthrography in the assessment of knee-joint problems, equally valuable to radiologists and the orthopaedic surgeon.

December 1980 170pp 21 line illus, 87 halftones
HB 0 412 21860 7 £12.00

Of related interest

Hip Arthrography

P Grech
1977 106pp illus
HB 0 412 15090 5 £12.50

Casualty Radiology

A Practical Guide for Radiological Diagnosis

P Grech, Consultant Radiologist, Northern General and Lodge Moor Hospitals, Sheffield.

Based on the extensive experience of a major casualty hospital, this highly illustrated book considers the more unusual diagnostic problems faced by the casualty officer and radiologist. Although principally concerned with fractures, it also includes a chapter on foreign bodies.

January 1981 256pp 276 halftones
HB 0 412 22740 1 £15.00

Nuclear Medicine Communications

Editors
K E Britton, St Bartholomew's Hospital
P J Ell, Middlesex Hospital
R F Jewkes, Charing Cross Hospital

This new journal provides an international forum for the rapid publication of significant new developments in the nuclear medicine field. It is published in association with the British Nuclear Medicine Society.

Full details are available from the publisher

Special Issue of Nuclear Medicine Communications
Quality Assurance of Radiopharmaceuticals

Edited by **M Frier** and **S R Hesslewood,** Addenbrooke's Hospital, Cambridge.

The contributors provide practical guidelines for quality control of hospital-produced radiopharmaceuticals for use in nuclear medicine procedures. Written by a group of experienced radiopharmacists, this book should be of great value to all who use radioisotopes in the investigation of disease.

December 1980 64pp illus.
PB 0 412 23270 7 £4.50

Chapman & Hall Ltd. 11 New Fetter Lane London EC4P 4EE

Radiology of Iatrogenic Disorders

Series Editors: **M.A. Meyers, G.G. Gharemani**

Iatrogenic Gastrointestinal Complications

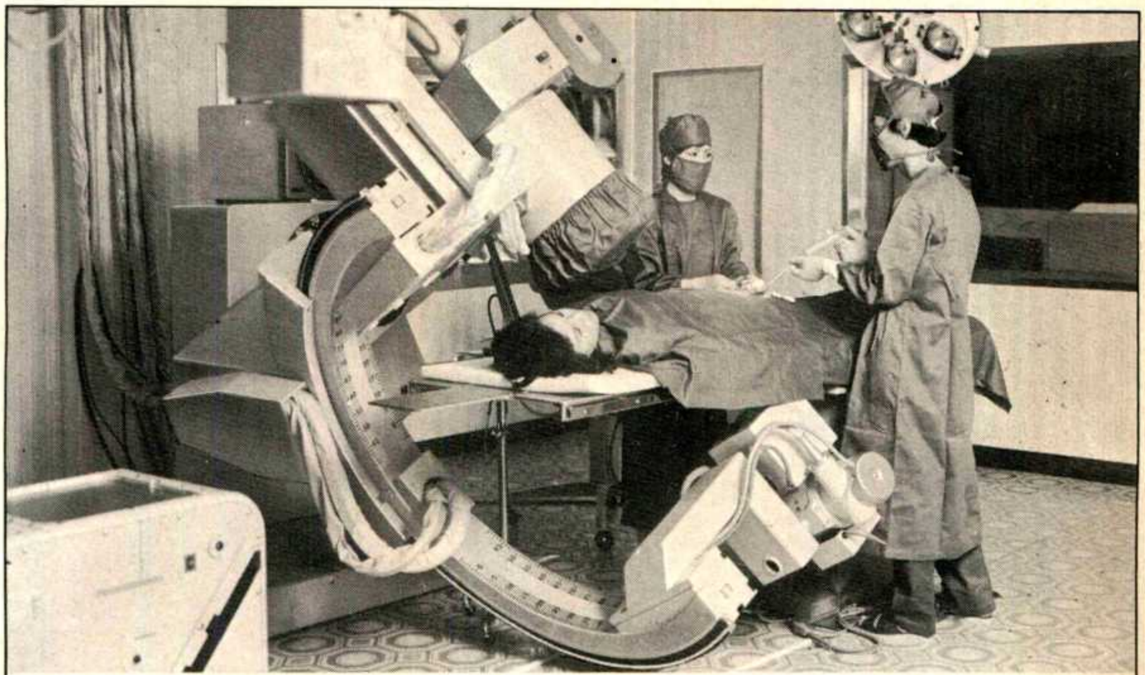
Editors:
Morton A. Meyers, State University of New York at Stony Brook;
Gary G. Gharemani, Evanston Hospital - Northwestern University

1981. 507 figures. XIII, 306 pages
Cloth DM 99,50; approx. US $ 47.40
ISBN 3-540-90505-7

The dramatic increase in the number of modern diagnostic and therapeutic methods at the physician's disposal has led to a broader spectrum of iatrogenic disorders affecting the digestive organs. This timely volume is an unprecedented survey of the underlying mechanisms and clinical and radiographic features of iatrogenic disorders of the gastrointestinal system. Contributions by highly respected authorities provide detailed, illustrative coverage of the role of radiology in the diagnosis and treatment of complications resulting from surgery, drug therapy, endoscopy, radiology and radiation therapy. High-quality radiographs and selected references that guide the reader to relevant journal literature accompany the text, making this a truly unique reference work.

This contemporary new series comprehensively assesses and details the broad spectrum of mechanisms and effects of disorders that result from the use of acceptable diagnostic and therapeutic procedures. Radiologic documentation is viewed here as a critical tool to aid in uncovering and/or in confirming the presence and severity of many iatrogenic complications.
Each book in this five-volume series contains illustrations to fully enhance the power of visual instruction. Individual volumes will deal with the role of radiologic documentation in iatrogenic pediatric, thoracic, urologic and skeletal complications, in addition to the volume on gastrointestinal complications described above.

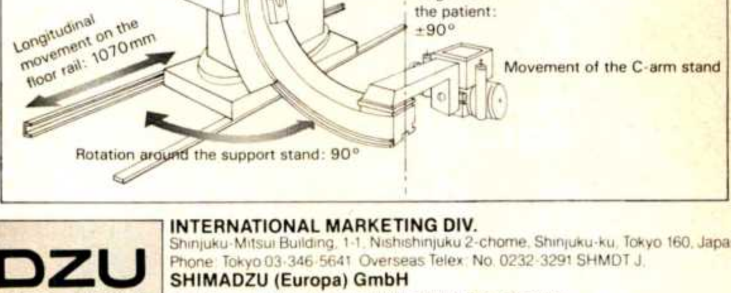
Springer-Verlag
Berlin
Heidelberg
New York



New Shimadzu C.V.S. & Angiography System

The new, versatile MH-10 System is designed around a uniquely engineered "iso-centric" C-arm which provides a full range of three-dimensional movements.

Once set the unique C-arm system maintains a constant SID (Source-Image receptor Distance) that assures sharp multi-directional cinefluorographic and radiographic images. Additionally, the RF-30 Automatic Collimator can be used to keep the irradiation field a constant size even when changing the SID or viewing field of the image amplifier. This further permits effective fluoroscopy and cinefluorography at low X-ray dosages. Two OAT stands can be used; one for holding the film changer (up to 2X magnification) and the other to additionally hold the 2-directional X-ray assemblies (frontal and lateral). A PUCK film changer which provides up to 3X magnification can also be incorporated. Two kinds of catheterization tables can be chosen; the KS-40 which is just 5mm thick and highly impervious to X-rays, thereby producing radiographs of excellent contrasts, or the KS-40F frameless tabletop for fluoroscopy and cinefluorography.


Tilting for 'sagittal view' radiograph: ±45°
Movement of the image amplifier: 300mm
±90°
Rotation around the long axis of the patient: ±90°
Longitudinal movement on the floor rail: 1070mm
Movement of the C-arm stand
Rotation around the support stand: 90°

SHIMADZU
CORPORATION KYOTO JAPAN

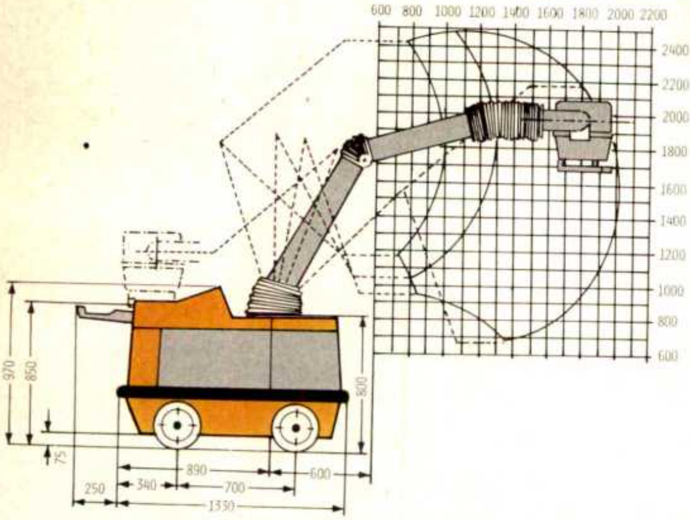
INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Dusseldorf 1, Johannes Weyer Str 1 F.R. Germany
Phone (0211) 314061 Telex 08586839 SHIM D
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone 01-902-6098 ENGLAND

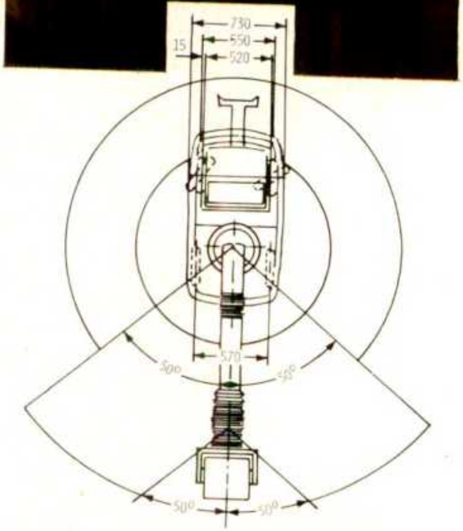
SIEMENS

Mobil XR – brings a microprocessor controlled, aseptic mobile radiography unit to the patient.

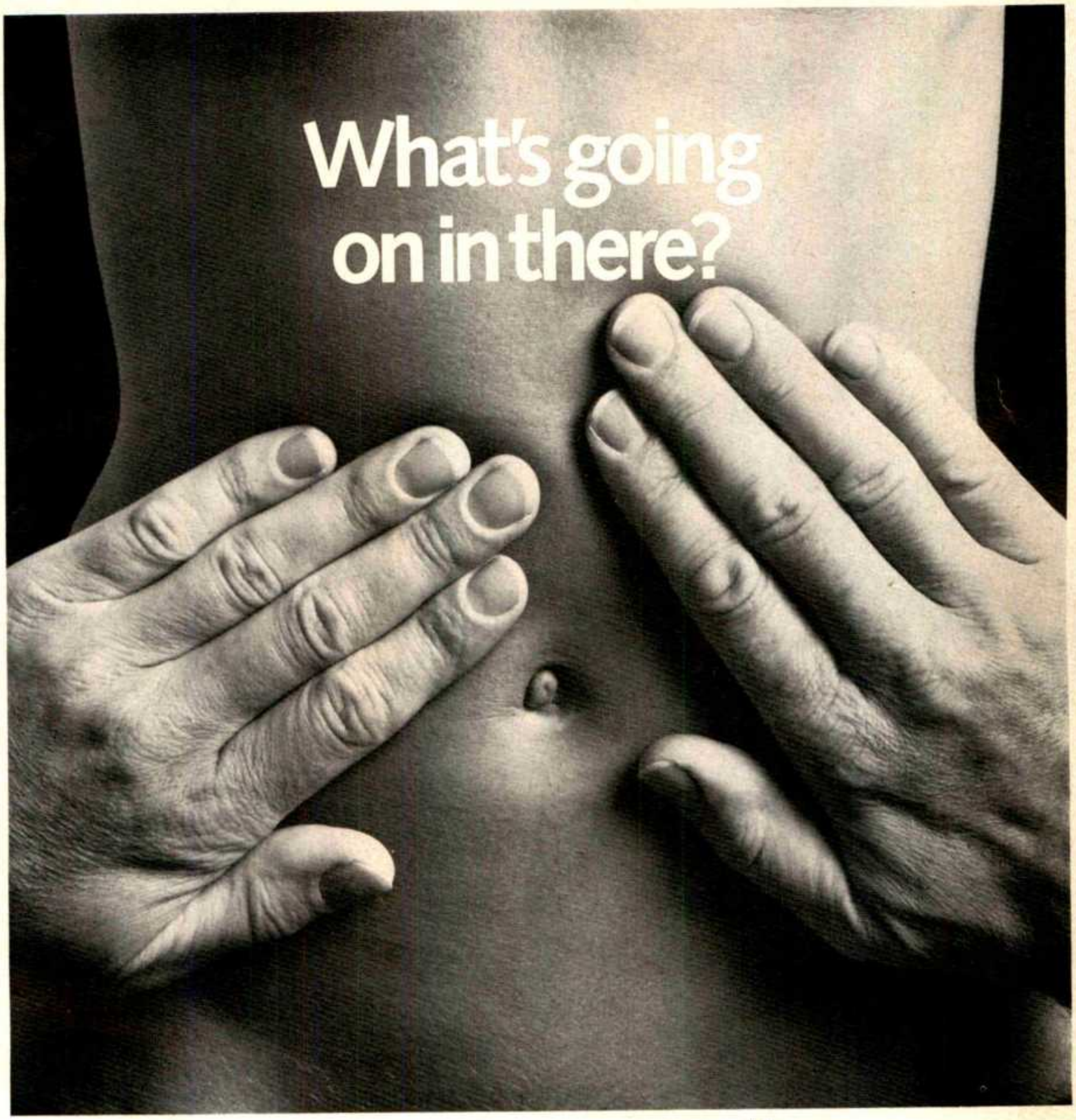
The battery-powered MOBIL XR is self-propelled and self-contained with microprocessor controls providing full power exposures at 20 kW time after time. The adjustable counter-balance arm and a wide range of alphanumerically displayed exposure parameters allow sharp image examination of any organ or limb. Aseptic design with touch controls and total enclosure fo all components make it ideal for theatre use. Infinitely variable speed control makes it easy to manoeuvre and pull-out cable allows simple recharging at any power point.

For further details or a demonstration contact:
Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS.
Tel. Sunbury (09327) 85691.





In the world of mobile radiography Siemens has the answer.


What's going on in there?

Trust baritop to tell you

Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.

ADVANCES IN ECHOCARDIOGRAPHY

Co-organizers – Drs. S. Hunter and R. Pridie.

Venue: Freeman Hospital, Newcastle upon Tyne.

Date: 28th September to 2nd October 1981.

The Biannual Course in Echocardiography will be held on the above dates in the Cardiothoracic Centre at Freeman Hospital, Freeman Road, Newcastle upon Tyne. It is a five day residential course and accommodation will be booked at reasonable cost, in a local hotel quite close to the hospital. The fee for the course is £75·00. It is hoped that the teachers on the course will include, in addition to the organizers, Dr. Derek Gibson, Mr. Graham Leech, Dr. Michael Godman, Dr. Roger Hall, Dr. Keith Evemy and Dr. George Sutherland. All aspects of echocardiography will be touched on in the course, and a period of each afternoon will be set aside for practical demonstrations. It is anticipated that all course participants will have had some experience of echocardiography previously.

Enquiries and booking should be made through Mrs. Maureen Johnston, Department of Paediatric Cardiology before 1st August 1981.

New Zealand

AUCKLAND HOSPITAL BOARD

Applications are invited from suitably qualified Medical Practitioners for the position of:

Fellow in Cardiovascular Radiology

Green Lane Hospital

(available from 1 February 1982)

This is a training post designated as either Registrar or Specialist and would be suitable for applicants wishing to gain further supervised experience in cardiovascular radiology in a hospital of world renown.

Initial appointment is for a period of up to twelve months with provision for appointment for a further period not to exceed an aggregate of two years.

Applicants should hold a Radiological qualification, but applications from candidates with experience in Cardiology would be considered.

The salary will be in accordance with qualifications and experience within the scale of either:

Registrar NZ$20,216–27,127
or
Specialist NZ$30,630–38,341
plus additional payment for
hours worked in excess of 40
per week.

Conditions of Appointment, Form of Application and Explanatory Memorandum may be obtained from: The High Commissioner for New Zealand, New Zealand House, The Haymarket, London SW1Y 4TQ, ENGLAND.

Applications will close on Friday, 31st July, 1981 with: The Chief Executive, Auckland Hospital Board, P.O. Box 5546, Auckland 1, NEW ZEALAND.

Computerized Tomographic Scanners in Radiotherapy in Europe

Edited by Roger J. Berry

British Journal of Radiology
Supplement 15

Under the auspices of the Commission Informatique of the European Association of Radiology, a Workshop was held at the Headquarters of WHO, Geneva, from 28 to 30 March 1979 on 'The Use of Computerized Tomographic Scanners in Radiotherapy in Europe'. It was clear from the first that CT scanning would have a major impact on radiotherapy, but how and where? At this meeting 150 experts from 17 countries met to review, from a real background in clinical experience of using CT scanners in radiotherapy planning, the progress which had been made and the costs involved. CT scanning is not inexpensive, but the information provided is in many cases unique. Following a keynote address by Professor Brian Pullan of the University of Manchester outlining what is and is not likely to be possible in future in tumour imaging, the papers cover the practical use of CT scan information in assessing tumour volume, planning radiotherapy and following tumour response in the head and neck, the thorax and the abdomen. The linkage of CT information to radiotherapy treatment planning is discussed, and the way indicated towards true three-dimensional radiotherapy planning. All the papers presented at the Meeting are included in abridged form as well as rapporteurs' reports of the discussions in each section.

Orders to:

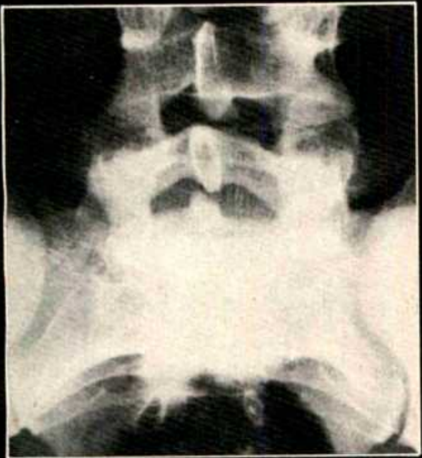
Publications, The British Institute of Radiology, 32 Welbeck Street,
London W1M 7PG

Price £19·50

ISBN 0 905749 09 X
ISSN 0007 1285

THE 3M TRIMAX SYSTEM:

THREE WAYS BETTER



1. Finer diagnostic quality.
The gadolinium oxysulphide formulation used exclusively by the 3M Trimax System ensures:
a) better definition from this high efficiency phosphor
b) less graininess from a finer, more regular grain structure
c) better image characteristics by reduced probability of scatter.

2. Less exposure time.
The Trimax System is faster - up to 90% faster than conventional systems. This means:
a) less radiation dosage,
b) less chance of patient movement,
c) greater use of fine focus.

3. Longer operating lif
Trimax screens, the first of which we introduced in 1974, have yet to shov any loss of speed.

That's why they all come with an exclusive 7-year guarantee against loss of speed.

That's why replacement ceases tc be a factor with the Trimax System.

When it comes to rare-earth x-ray systems, there's only one which offers a fully comprehensive range of screens and films, designed to outperform all the others on the three most critical parameters of: diagnostic quality, radiation dosage and long-term economy.

3M Trimax System. The most versatile, comprehensive and durable rare-earth system available. Specify it with confidence.

For further information about the Trimax Syster from 3M - the leaders in rare-earth phosphor technology - contact: Alan Budge, X-Ray Products, 3 United Kingdom Ltd, 3M House, PO Box 1, Brackne Berks, RG12 1JU. Telephone Bracknell (0344) 58458

3M and Trimax are trade m

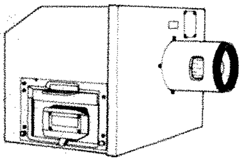
Oldelft offers you more than just a good camera... it gives you a complete system.

Oldelft makes high quality 100mm cameras for image intensifier photography and CRT display recording. But that's not all. Oldelft also makes a whole range of products that simplify the entire film handling operation after exposure. Together, these products make up the Oldelft 100mm daylight system. It's based on the use of 10x10cm sheetfilm. But mainly it uses apparatus already available in radiological departments. Which means it fits smoothly into the department's work routine. Nothing has to be changed.

Advantages of the 100mm sheetfilm system

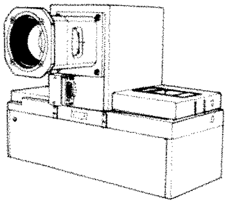
- the 100mm system works with sheetfilm - as you are used to in large-size radiography - which makes for easy sorting and selection and an efficient working routine.
- it works with medium-size film, which enables diagnostic information to be interpreted with the naked eye. It also cuts film and chemical costs and reduces x-ray dose for both patient and doctor.
- it works with the daylight magazine technique: its supply and take-up magazine hold enough film for a complete examination. No interruptions. No fussing with cassettes. Result: less time needed for examinations; better throughput of patients.
- the 100mm system is flexible. Components can be chosen to suit a hospital's individual needs.

General x-ray diagnosis



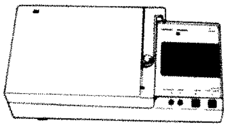
The Anodica-2 image intensifier camera is capable of up to two exposures per second. It is especially suitable for use in cases of gastro-enterology, neurology, urology, orthopaedics, gynaecology and paediatrics. Anodica techniques offset the disadvantages experienced with conventional large format radiography. Handling operations are considerably reduced and there is a marked increase in throughput of patients.

Special x-ray procedures

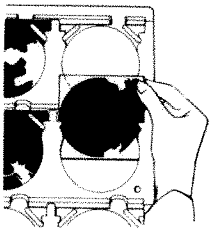


The high exposure rate of the Anodica HS - up to 12 exposures per second - offers great advantages in examinations such as general and selective angiography, cerebralangiography. Motion blur is reduced, focal spot of the x-ray tube is smaller and x-ray dose is low. Use of Anodica exposure technique means that catheterization and image intensification can be simultaneous. It is therefore not necessary to move the patient.

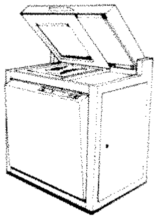
CRT display photography



With the Catodica camera-back for CRT display recording of ultrasound, gamma cameras and CT scanners, a substantially better quality image is obtained than is possible on positive paper film from instant camera-backs. The Catodica works with a magazine that can be loaded in full daylight. The automatic film transport means great facility and quick examination.

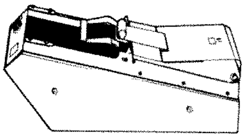


Film copying



The Delcomat provides a highly efficient copying service so that the exposures always remain at the radiological department. It gives top quality copies of large radiographs, complete or in part on 100mm sheetfilm. It also duplicates 100mm exposures on 1:1 scale. The Delcomat saves filing space and provides a basis for a teaching file.

Processing

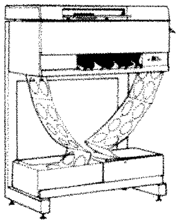


By means of the Film Feeder, 100mm sheetfilms can be processed automatically and in daylight, using normal large-size film processors without modification. Small daylight processors for instant use with the camera are also available.

Viewing

For quick quality check and easy diagnosis, exposures can be mounted in correct order in the Cadrix, a simple plastic holder, which is placed on the viewing box. For large group discussion, as for example during teaching sessions, pictures can be enlarged through the Heliomat viewer or by means of an overhead projector.

Framing



The manually operated Delcadro offers a simple method of mounting six exposures together in an economical paper frame. In this way pictures selected after viewing in the Cadrix can be kept together for orderly presentation and are readily filed. An automatic version of the Delcadro is also available. It is especially effective for handling large quantities of film.

In brief

The 100mm system offers an efficient method of picture registration for a large number of hospital examination areas. It reduces cost, saves time. For simple film handling, a sophisticated package of accessories is available. And remember - 100mm film offers a basis for planning substantial reduction in filing space.

Oldelft nv Optische Industrie De Oude Delft

Holland, Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011
U.S.A. Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, telex 089-2759

Please send me more information about the 100mm system.
I am particularly interested in:

☐ how to cut film costs	☐ 100mm spot film photography
☐ standardization on 10x10 film	☐ 100mm CRT photography
☐ filing space reduction	☐ 100mm copying services

Name ____________________

Address ____________________

City ____________________

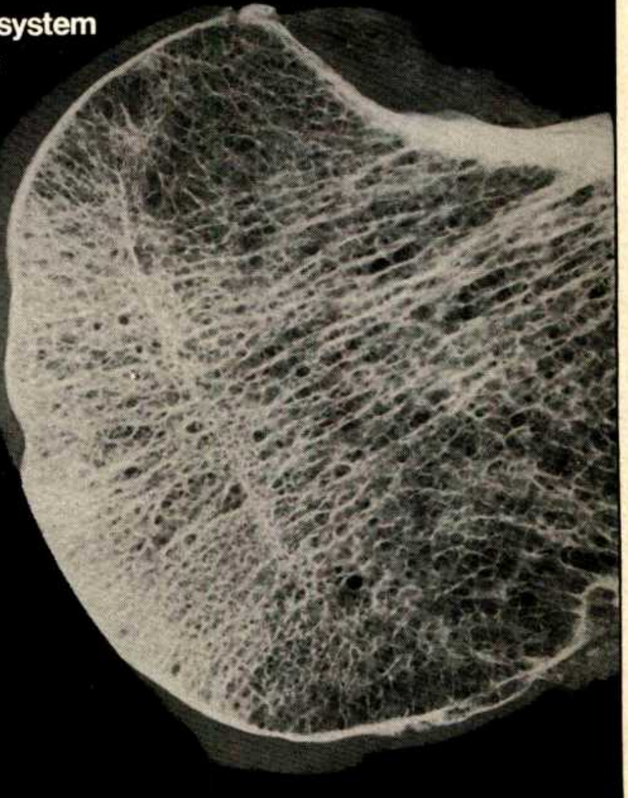
Country ____________________ 3

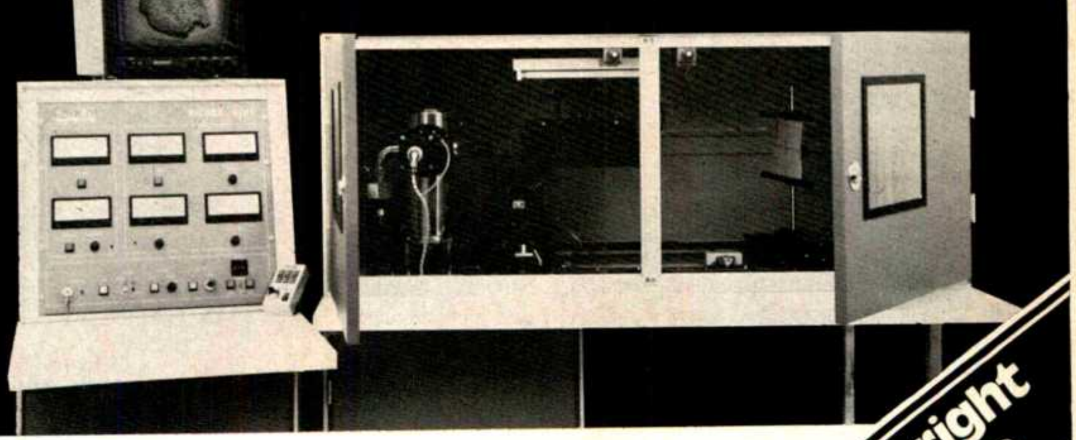
The new Nicolet Microx
Unique high definition Radiography

A completely united radiography system for imaging internal microscopic detail with infinite depth of field.

Discover the Microx difference

- High resolution 0·01mm
- Various magnification with zoom control of up to 25 times on film and 100 times on TV
- Thick sample capability
- No sample preparation
- Instant dynamic viewing on TV display
- Permanent high resolution photographic record with X-Ray or Polaroid film
- Stereo photography for three-dimensional viewing
- Large sample handling capacity
- Ample space for the addition of special sample handling devices
- Easy to use





Nicolet Instruments Limited
A NICOLET INSTRUMENT SUBSIDIARY
Budbrooke Road, Warwick, England, CV34 5XH Tel: (0926) 44111 Telex: 311135

Get it right 1st time

16-18 September 1981
London

Conference and
Trade Exhibition

Paediatric Cardiology
1981

Organising Committee:
Prof. R. H. Anderson, Dr. E. A. Shinebourne,
Prof. F. J. Macartney, Dr. M. Tynan.

Sponsored by the British Heart Foundation
Speakers will include: S. Howarth, A. Pacifico,
M. Paul, J. Somerville, M. Yacoub, A. Becker,
O. Scott, D. Heath, M. Godman, J. Taylor, D. Southall,
D. Krickler, D. Ward, G. Thiene, J. Stark,
A. Carpentier, J. Wilkinson, J. Lincoln,
E. Gussenhoven, L. Allan, D. Gibson, G. Miller,
P. Deverall, S. Hunter, M. Quero Jimenez, E. Silove,
M. de Leval, A. Bentovim, D. Silverman, N. Dennis,
A. Blancquaert, B. Keeton.

A reduced fee is available for Nurses and Radiology Technicians.

For further information:
Conference Services Ltd., 3 Bute Street,
London SW7 3EY, UK.
Tel: 01–584 4226. Telex: 916054 JOYBRI.

Computers
Two BIR Special Reports

Considerations about the use of computers in radiodiagnostic departments
BIR Special Report 14
Edited by Professor G. H. du Boulay. 1977
SPECIAL PRICE: £1·00

Computers in the control of treatment units
BIR Special Report 16
By a multi-disciplinary task group convened
by R. E. Bentley. 1979
PRICE: £2·40

Orders to:
The British Institute of Radiology
32 Welbeck Street
London W1M 7PG
ISSN 0306–2120

SOUTHERN ALBERTA CANCER CENTRE
CALGARY, ALBERTA

Director of Radiation Oncology

The Provincial Cancer Hospitals Board is seeking a Director for the Department of Radiation Oncology for September 1st, 1981, for the new Southern Alberta Cancer Centre in Calgary. Salary scales are competitive and negotiable on the basis of qualifications and experience. Academic cross-appointments with the University of Calgary Medical School provide opportunity for teaching and research. Research is supported by the Alberta Heritage Fund and by a population based tumor registry.

Positions are available to the Director for recruiting additional radiotherapists to the current staff of five. A full staff of physicians, treatment planners, mould room personnel and a workshop team now exists. The technologist complement is currently full and planned to expand when the Centre moves to its new facilities in the fall of 1981.

The Centre handles over 2500 new cancer patients, 18,000 out-patients visit and over 20,000 radiotherapy visits yearly. Present facilities include a 6 MeV Accelerator, two Cobalt 60 Units and a superficial X-ray machine. In addition a 20 MeV Linear Accelerator and a third Cobalt 60 Unit will be installed in the new Centre along with a second Simulator.

The new Cancer Centre provides comprehensive cancer care for Southern Alberta which has a population of about one million. Calgary, situated near the Rocky Mountains, is a rapidly growing financial and oil centre in the Canadian West. It has a population of about 550,000 with four major hospitals served by the Cancer Centre.

For further information please reply in confidence to:

Dr. L. Martin Jerry, Director,
Southern Alberta Cancer Centre, 2104 – 2nd Street S.W.,
CALGARY, Alberta. T5S 1S5
Telephone Number: 403–263–0770

SIEMENS

Multigraph.
Versatility in Tomography
from Siemens.

The MULTIGRAPH is an X-ray diagnostic u
for planigraphy and Bucky radiography on
recumbent patients.

The unit permits the preparation of planigra
with linear, elliptical and spiral blurring, spira
blurring being particularly advantageous fo
objects with high image contrasts (head,
skeletal planigraphs), multiple superimposi
(temperomandibular joint) and strongly
interfering bodies close to the object
(petrous bone).

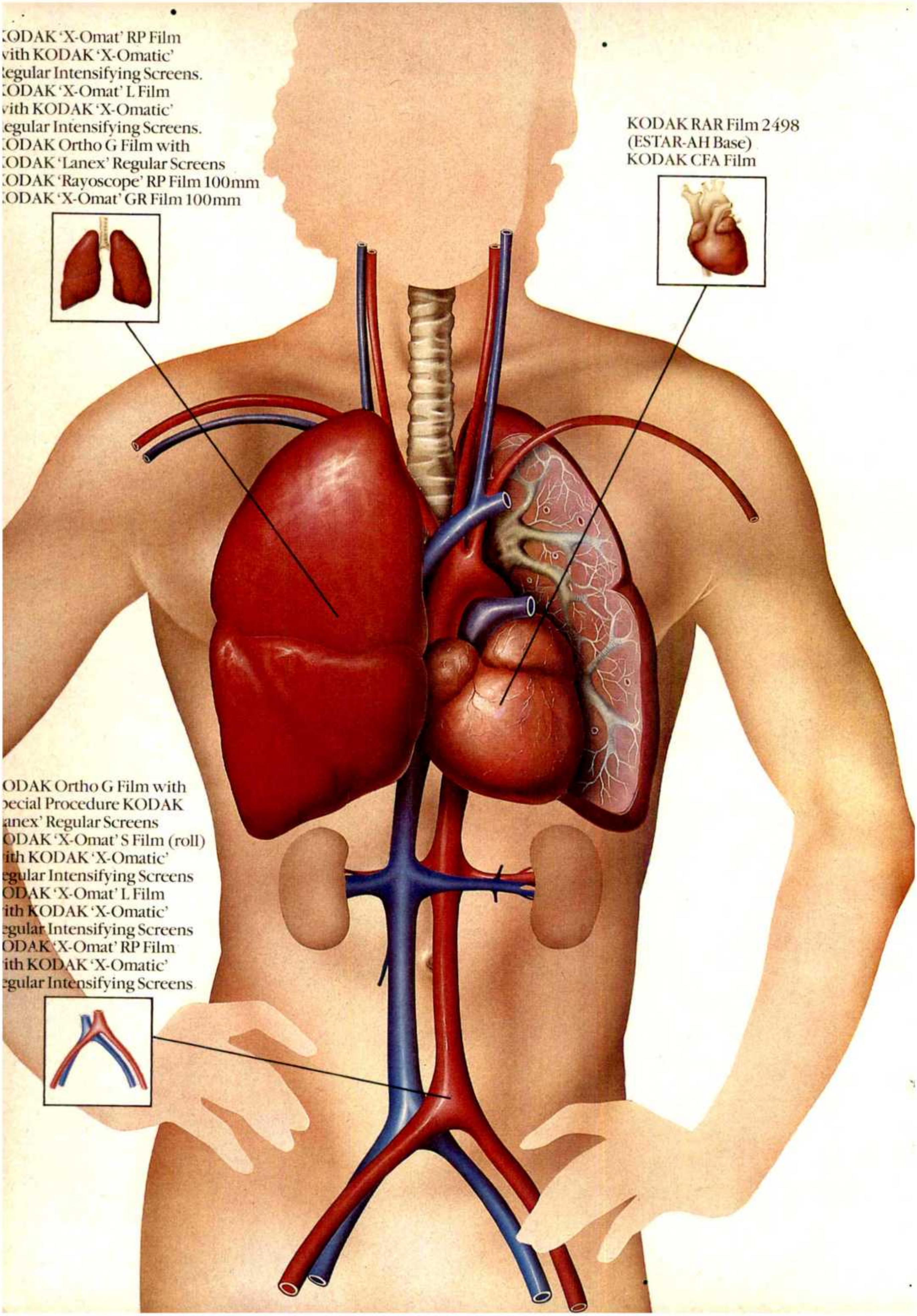
Zonography with linear and circular blurrin
and Bucky radiography with vertical and
oblique beam projection supplement the
versatile application.

Special Features

- Complete floor clearance through use of a ceiling support.
- Possibility for all erect Bucky radiography e.g. routine chest and lumbar spine.
- Radiography in bed or on a trolley in front of the unit.
- Facility for lateral views to be taken from both sides of the table.
- Rotatable Bucky grid automatically centered onto focus.

For further information please contact:
Siemens Medical Group, Siemens Limite
Windmill Road, Sunbury-on-Thames.
Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691

In the world of radiographic equipment,
Siemens has the answer



KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK 'X-Omat' L Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK Ortho G Film with
KODAK 'Lanex' Regular Screens
KODAK 'Rayoscope' RP Film 100mm
KODAK 'X-Omat' GR Film 100mm

KODAK RAR Film 2498
(ESTAR-AH Base)
KODAK CFA Film

ODAK Ortho G Film with
pecial Procedure KODAK
anex' Regular Screens
ODAK 'X-Omat' S Film (roll)
ith KODAK 'X-Omatic'
egular Intensifying Screens
ODAK 'X-Omat' L Film
ith KODAK 'X-Omatic'
egular Intensifying Screens
ODAK 'X-Omat' RP Film
ith KODAK 'X-Omatic'
egular Intensifying Screens

An outline of Kodak products for cardio-vascular examination.

Kodak has the most comprehensive service network in the country.

We back that service with a range of products that includes over thirty diagnostic imaging films; and covers processors, cassettes, intensifying screens, chemicals and daylight handling equipment.

Kodak Service is there to help you maintain consistent image quality.

In the working environment, this means we can aid with planning an efficient process area.

In human terms, we can help with the training of radiologists, radiographers and technicians: on your premises or at our own Marketing Education Centre.

Equipment maintenance is also an important quality control factor, and Kodak provides a highly competitive service from strategically located Sales Centres.

For details, speak to your Kodak representative.

He can give you up-to-date information on all areas of diagnostic imaging.

Kodak. We care about your image.

Kodak

KODAK 'Lanex' Regular Screens for special procedures are available to fit Puck, AOT and CGR rapid film changers. Kodak and all product names printed thus–'X-Omat'–are trade marks.

APPEAL

A permanent home for British radiology

The Appeal Committee

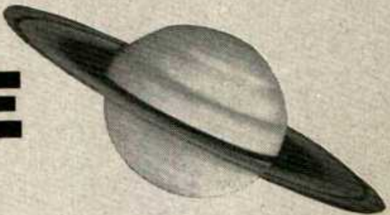
Sir Jan Lewando, CBE (*Chairman*)
Professor G. H. du Boulay (*Appeal Co-Ordinator*)
Mr. L. F. Barr Smith
Dr. Julian Bloom
Sir Richard Doll, OBE, FRS
Mr. Kevin Hughes, OBE
Professor L. F. Lamerton
Sir Thomas Lodge
Dr. J. F. Loutit, CBE, FRS
Professor W. V. Mayneord, CBE, FRS
Professor J. H. Middlemiss, CMG
The Lord Penney, OM, KBE, FRS
Sir Edward E. Pochin, CBE
Sir John Read
Mr. C. F. E. Shakerley
Professor Sir David Smithers
Professor R. E. Steiner, CBE
Dr. Herman D. Suit
Dame Janet Vaughan, FRS
Professor Sir Brian Windeyer
The Lord Zuckerman, OM, KCB, FRS

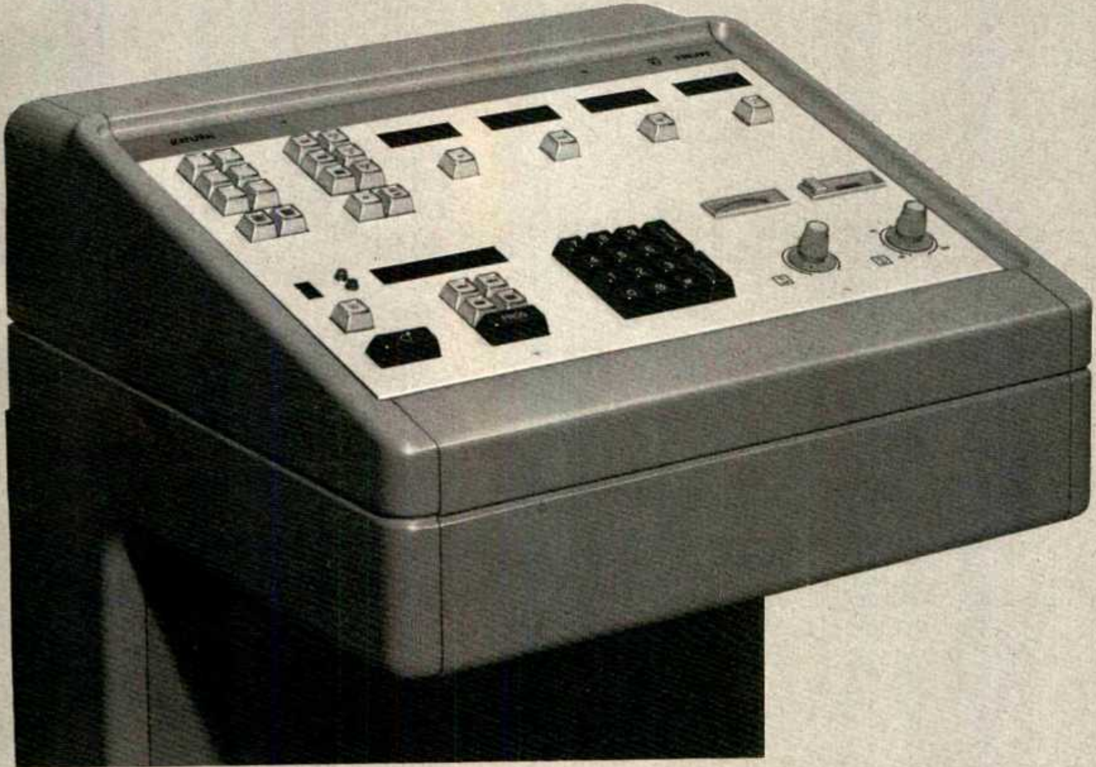
The President of the Institute and Appeal Executive Committee members

Funds are still needed for the new permanent home for The British Institute of Radiology at 36 Portland Place, London W1, next door to the Royal College of Radiologists

Donations and ideas to:
Appeal Co-Ordinator, 32 Welbeck Street, London W1M 7PG (01–486 5084)

THE COMPUTERIZED GENERATOR OF TOMORROW IS HERE TODAY





SATURN— THE MICROPROCESSOR CONTROLLED GENERATOR

FLEXIBILITY

- One, two or three factor control
- Operator input to memory store
- Over 200 operator introduced programmes
- Last exposure on each auxiliary memorised for instant recall

DIGITALLY DISPLAYED

- kV mA mAs time
- Post exposure of mAs and time
- Organ and projection
- Number of further exposures possible
- Diagnosed error or malfunction

PHILIPS

PHILIPS **Medical Systems**

Kelvin House, 63/75 Glenthorne Road

The London Ultrasound Course for Radiologists

October 19th–23rd 1981

This course in clinical ultrasound is designed to cover non-obstetric abdominal scanning in depth, but will also include certain other applications. The course will be held in a London hotel and will be limited to 50 participants.

Course leaders:–

David Cosgrove Keith Dewbury Hylton Meire

Further information from:–

Dr. H. B. Meire, Clinical Research Centre, Harrow, Middlesex
HA1 3UJ
UK

RADIOLOGIST

£38,000 PLUS

CANADA

We have been asked to assist in locating a professionally qualified Radiologist to develop and head a practice in a new 300 bed hospital, which is one of the most modern in Western Canada, located in a community of 30,000 serving Alberta's rich tar sands.

Applications or enquiries are invited from individuals with professional credentials in radiology who are desirous of an autonomous working environment with the most up-to-date equipment available, coupled with the advantages of small city living in the centre of one of Canada's most buoyant economic regions.

Our client is offering a generous relocation/joining bonus and guaranteed remuneration of not less than £38,000 per year.

Interested doctors should write A. J. Martin or W. T. Lalonde, referring to Assignment #1021.

Executive Search Division
HicklingJohnston
Hickling-Johnston Limited, Management Consultants
415 Yonge Street, Toronto M5B 2E7, Canada
Telephone (416) 977-2811

TORONTO
MONTREAL
OTTAWA
EDMONTON
CALGARY

Member of the Canadian Association of Management Consultants

Ultrasound
in Medicine & Biology

Official Journal of the World Federation
for Ultrasound in Medicine and Biology

Editor: **DENIS N. WHITE,**
Queen's University, Ontario

The journal publishes original articles dealing with the interaction of ultrasonic energy with living systems for the purpose of promoting new knowledge concerning the understanding and employment of this form of energy in medicine and biology. While it is recognized that this includes a broad range of topics, it is expected, because of current needs and emphasis, that the majority of the published pages will deal with ultrasonic applications in clinical medicine. The journal aims to achieve high standards of quantitative reporting in the manuscripts that it publishes. Papers solely concerned with engineering techniques are appropriate only if the methodology, or the instrumentation described, are important in medicine or in biology. Only occasional review articles or articles of historical interest are published. In addition a section devoted to short Case Reports or Clinical or Technical Notes of 1000-2000 words in length is included. Letters to the Editor of 300-1000 words in length comprising (a) brief reports describing important preliminary results or new ideas, or (b) relevant comments on papers published in the journal or (c) relevant comments on issues of interest to the readership of the journal, are also published.

Subscription Information

Published quarterly
Annual subscription 1981 US$95.00 £43.18
Two-year rate 1981/82 US$180.50 £82.04
Prices include postage and insurance

Sterling prices applicable to UK and Eire customers
All prices subject to change without notice.

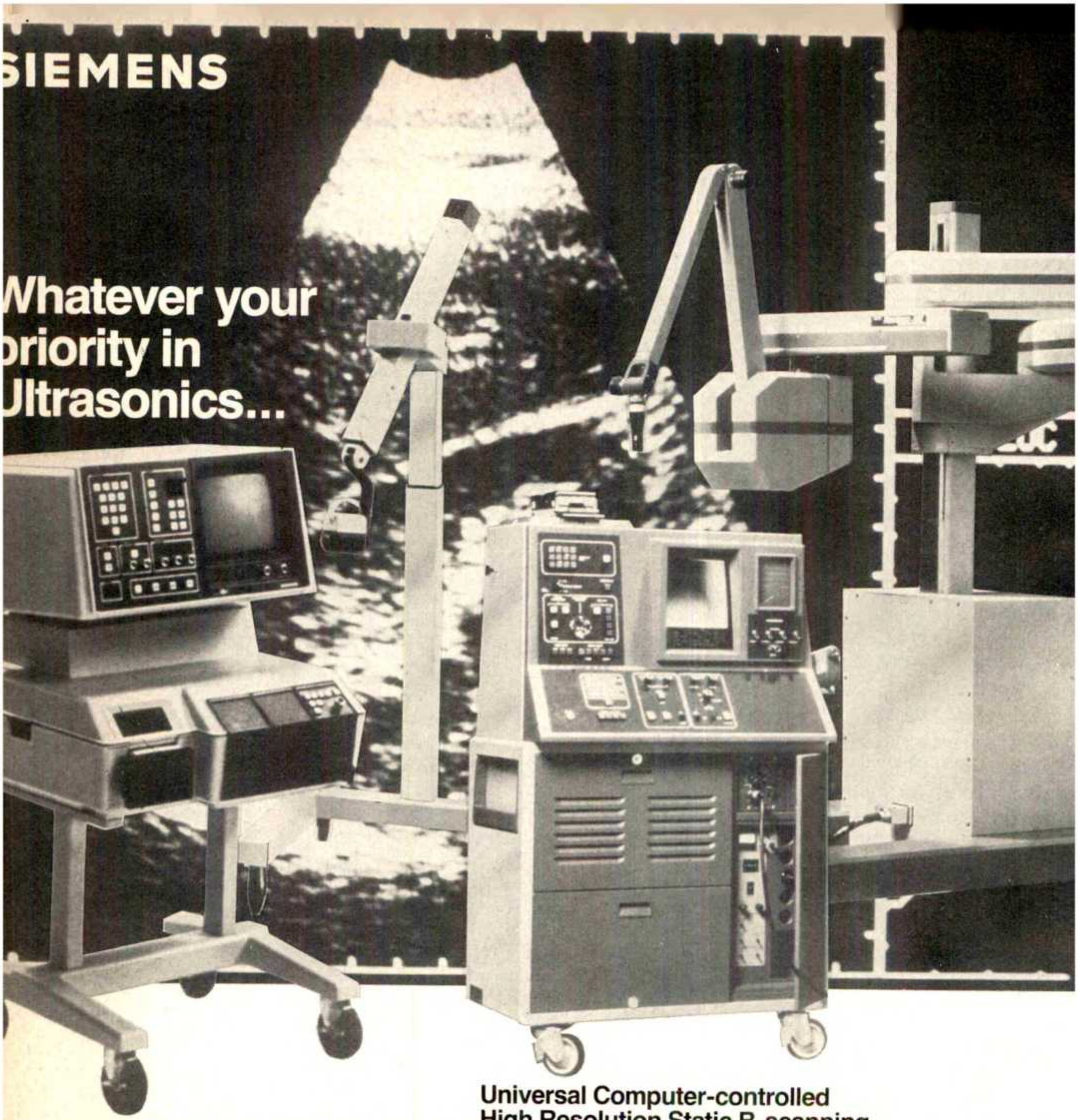
Free specimen copy gladly supplied on request.

Pergamon Press
Headington Hill Hall, Oxford OX3 0BW, England
Fairview Park, Elmsford, New York 10523, USA

8/80/1G/1

SIEMENS

Vhatever your riority in Jltrasonics...



utomatic, Computer-controlled Dynamic nd High Resolution Static B-scanning

e Sonography System RA-1 diagnostic ultra-sound anner uses sophisticated, computer-controlled age processing to achieve superior image resolution. e advanced, state-of-the-art scanheads comprise:
.FOV scanheads for multiformat abdominal anning.
VV scanheads for high frame-rate scanning.
Small parts scanhead, incorporating Doppler with ectral Analysis, for superficial vessel and organ studies, neonatal and paediatric scanning.
e modular design guards against obsolescence whilst mitting expansion and the ability to retrofit new aging techniques as they are developed.

Universal Computer-controlled High Resolution Static B-scanning

The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

- ❊ Wide range of transducers ❊ Image Process Functions
- ❊ Area, Circumference and Volume measurements.
- ❊ Obstetrics measurement facility ❊ Floppy disc interface

Future improvements to the image processing may be incorporated due to the flexible computer software.

Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner.
For full details write to: Siemens Medical Group, Siemens Limited, Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691.

.Siemens gives you the choice!

Forensic Radiology

By **K.T. Evans** MB, ChB, FRCR, FRCP, DMBD, FFR(RCSI)
Professor of Radiology, Welsh National School of Medicine

and **B. Knight** MD, BCh, FRCPath, DMJ
Reader in Forensic Radiology, Welsh National School of Medicine

This unique work surveys every aspect of the interface between radiology and the law, both in the application of radiological techniques to forensic problems, notably in identification and trauma, and in the legal aspects of clinical radiology, ranging from informed consent to malpractice. The hazards of radiological procedures and the medico-legal implications of diagnostic radiology are discussed, while the role of the radiologist in skeletal and dental identification is stressed.

July 1981. 160 pages, 110 illustrations.
About £15.00

Contents

Historical foreward
Radiology in identification
Radiology in forensic dentistry
Radiology in forensic pathology
Child abuse syndrome – the 'battered child'
Medico-legal implications of radiological procedures
Radiological mishaps and malpractice
Medico-legal aspects of radiology of trauma
Healing of fractures
Age range in the appearance of ossification centres and epiphyseal fusion

some other titles of related interest

Gynaecological Radiology

G.H. Whitehouse MB, BS, MRCP, FRCR. 1981.
248 pages, 257 illustrations. £24.00

As well as covering the more specific investigations relating to the genital tract, it is shown that other standard radiodiagnostic procedures and the recently introduced modalities of ultrasonography and computerised axial tomography, are applicable to the gynaecological patient.

Clinical Radiology in Gastroenterology

C.I. Bartram MB, MRCP, FRCR and Parveen Kumar MD, MRCP. 1981. 216 pages, 425 illustrations. £16.00

The role of radiology, including ultrasound and CT scanning, in disorders of the gastrointestinal tract, liver and pancreas, is analysed in this book.

Real-time Ultrasound in Obstetrics

Edited by M.J. Bennett MD, MRCOG, FCOG and S. Campbell MB, BS, FRCOG. 1980. 160 pages, 88 illustrations. £15.00

Nuclear Medicine: an Introductory Text

P.J. Ell MD, MSc, and E.S. Williams MD, PhD, FRCP. July 1981. 288 pages, 211 illustrations. About £16.50

This book informs radiologists, oncologists and clinicians of the wide range of nuclear medicine facilities and explains to those involved with radioactive materials the clinical relevance of their work.

X-ray Diagnosis

Peter Armstrong MB, BS, FRCR and Martin L. Wastie MB, BChir, MRCP, FRCR. 1981. 360 pages, 564 illustrations. £19.75

This title is designed as a textbook of diagnostic radiology for the medical student and newly qualified doctor. For each body system a number of basic signs are described and the differential diagnostic possibilities explored.

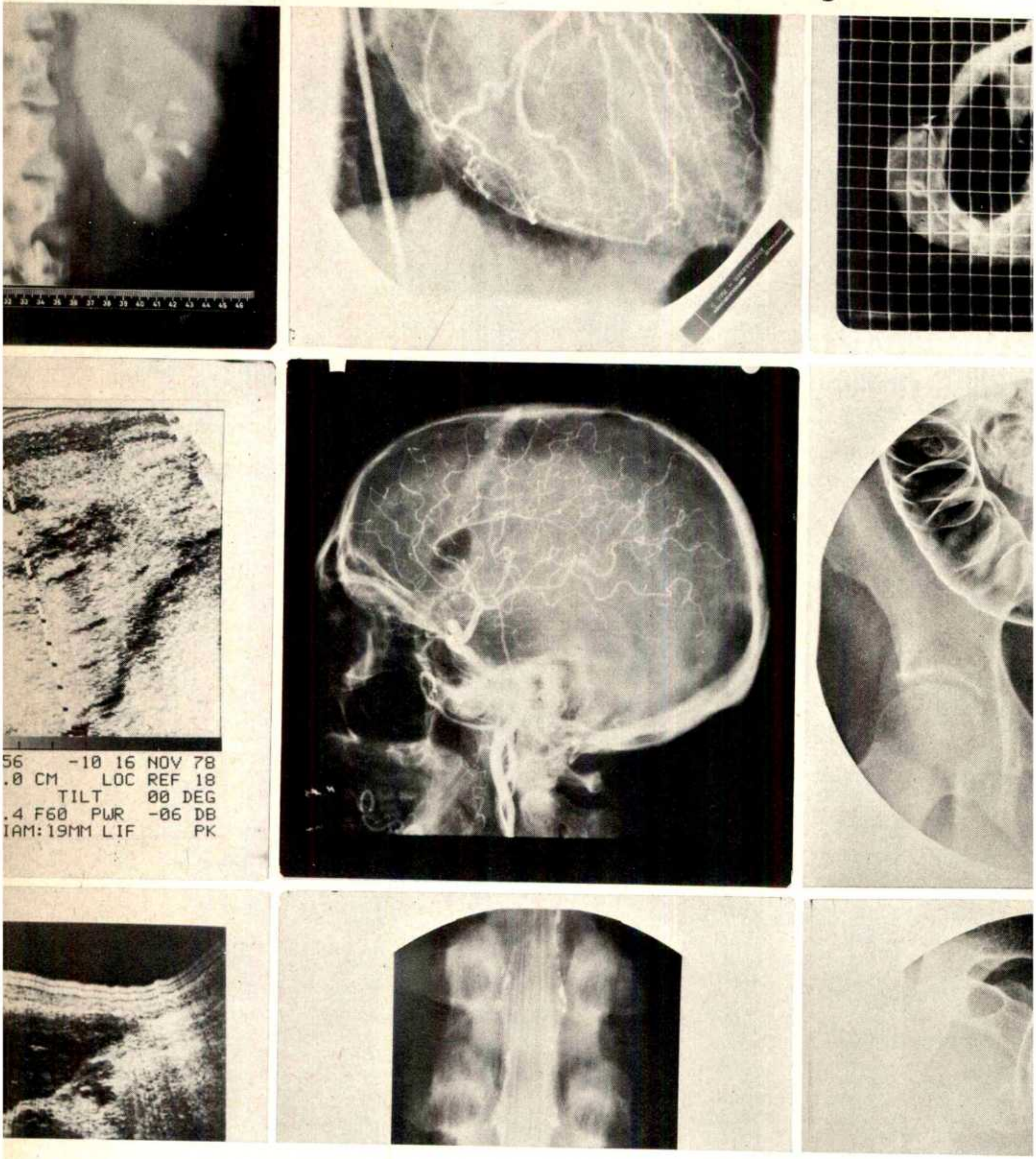
Uroradiology

Thomas Sherwood MA, MB, DCH, FRCP, FRCR. 1980. 360 pages, 435 illustrations. £35.00

Blackwell Scientific Publications

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY
C. U.

The Oldelft 100mm system is

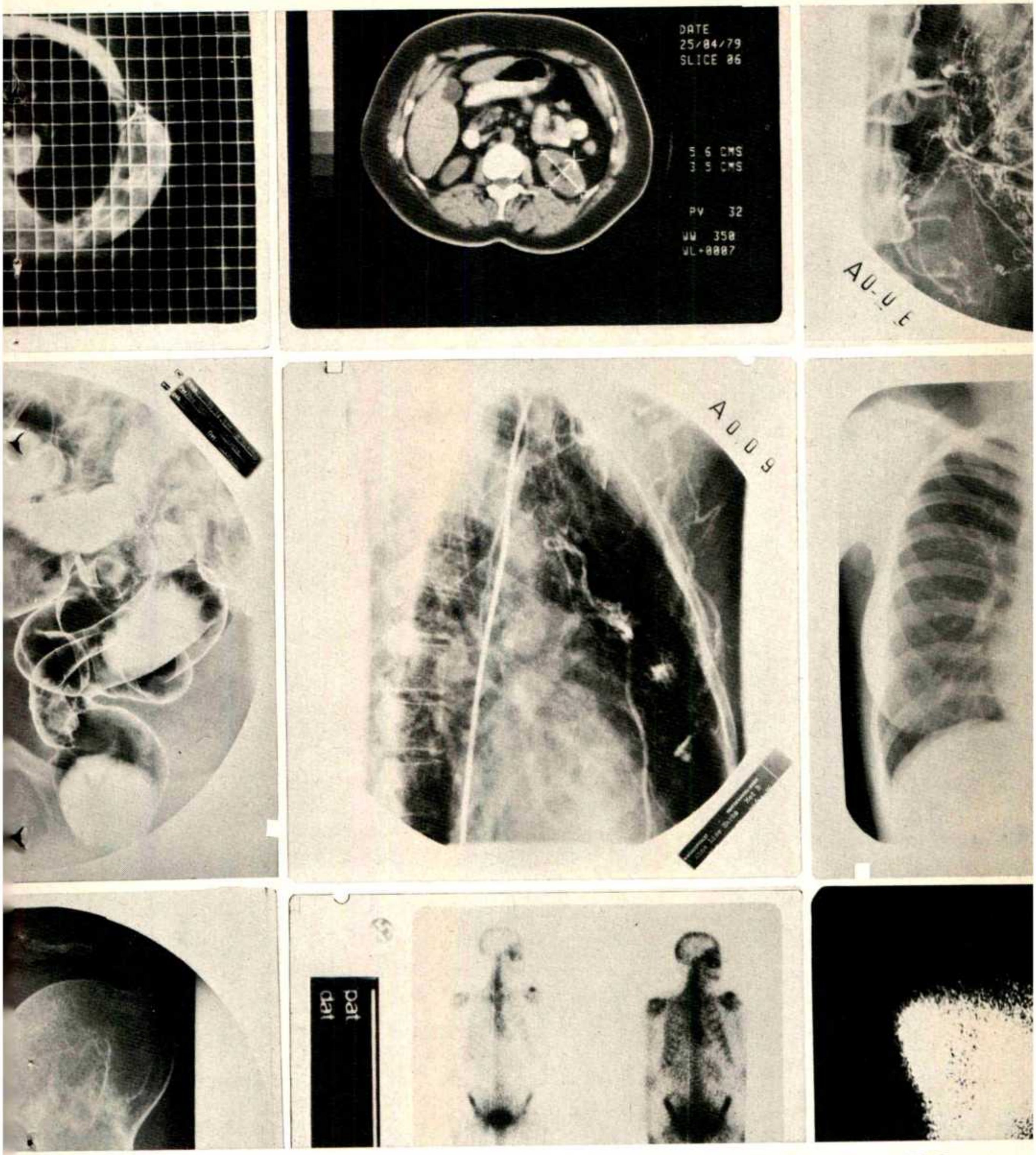


Only 10 x 10 cm sheet film offers standardization a chance –

*ıelft products are sold by the
ding x-ray equipment manufacturers*

Of course there are limits. It's not possible to achieve complete uniformity in a hospital radiology department.
Fortunately, a great deal of all diagnostic imaging can be standardized by adopting the Oldelft 100mm system.
It improves efficiency and makes for more effective use of equipment.
Handling is less complicated.
100mm System demands only 3 types of film: for CRT, image

more efficient and more economic



with up to 60% of your originals

intensifying and copying. In this way total filmstock can be easily reduced, using less film of different sizes and sensitivities.
The Oldelft 100mm system also saves valuable space in filing systems.
That's just one of the many attractive features of standardization.

Oldelft: quality and reliability.

Oldelft

nv Optische Industrie De Oude Delft

Holland, Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011

U.S.A., Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, tel

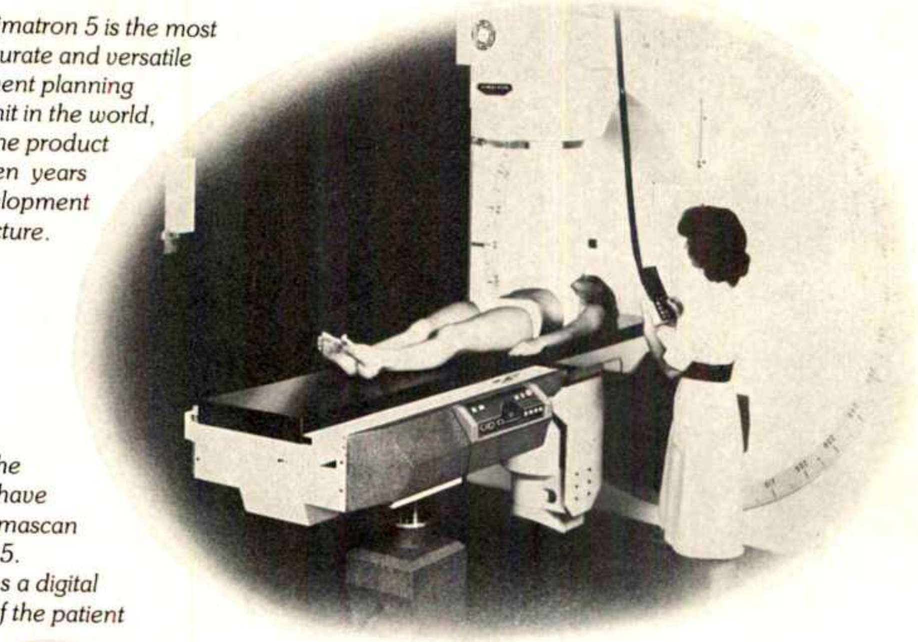
Germany, Postbox 5420, D 6300
Giessen/Lahn, Tel. (0641) 4 10 49, telex 4

Japan, Osaka, Postbox 1042

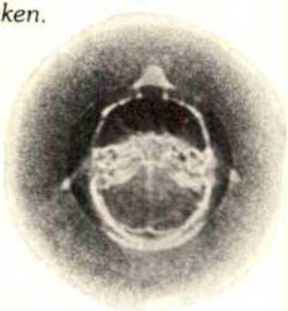
TEM

Ximatron 5
Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

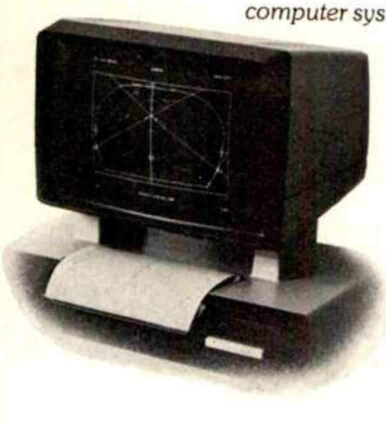


Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY

Radionuclide Tracer Techniques in Haematology

C S Bowring

Order today from your bookseller, or in case of difficulty from

Butterworths

Borough Green, Sevenoaks,
Kent, TN15 8PH, England.

Dr. Bowring's book will fill the need for a concise guide to the diagnostic uses of radionuclides in haematology. It deals with all the commonly used *in vivo* techniques, taking care throughout to provide practical information on their application. Those areas of haematology in which radionuclides are still developing are well covered, and for the reader with limited experience of nuclear medicine techniques there are two introductory chapters on basic physics and instrumentation.

Contents: Basic physics of radionuclides • Instrumentation • The measurement of red cell and plasma volume • Cell survival studies • Ferrokinetics • External counting • Imaging and applications of quantitative imaging • Absorption, loss and clearance studies • Appendices • Index

1981 148 pages 0 407 00183 2 **£8.50**

The Ontario Cancer Foundation
Ottawa Clinic

Applications are being invited for the post of RADIATION ONCOLOGIST in the Ottawa Clinic (Ottawa General Hospital Division) of the Ontario Cancer Foundation.

The Clinic registers approximately 2400 new cases of malignancy each year and about 1500 new cases were started on treatment in 1980.

The Ottawa General Hospital Division is located in the Ottawa University Health Science complex adjacent to the Medical School, National Defence Medical Centre and the Children's Hospital.

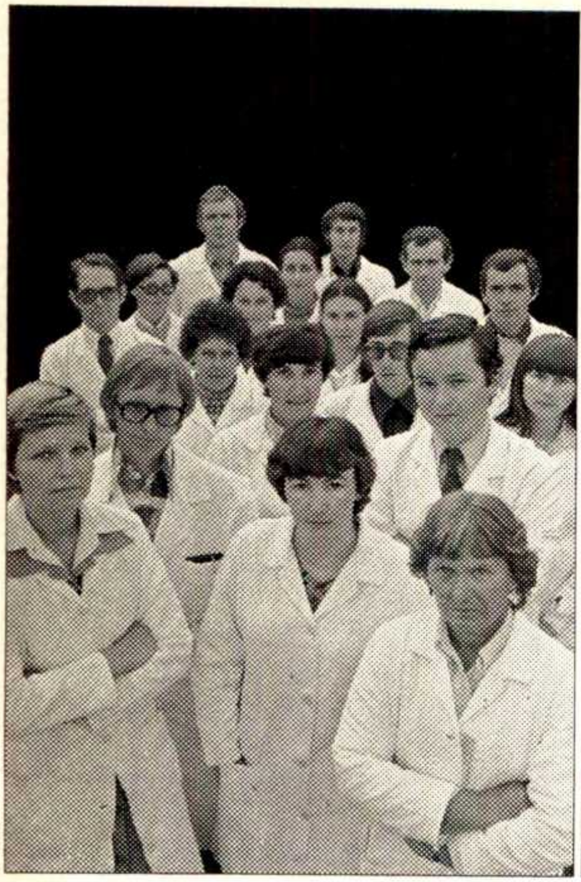
The combined equipment at the two divisions consists of a 20 MeV Linear Accelerator with electron capability; 6 MeV Linear Accelerator; two Theratron 780's and a Cobalt 78.

The Clinic has five radiation oncologists on staff and this position is to replace a radiation oncologist who will shortly be retiring in the General Hospital Division.

There are five medical oncologists and three physicists. The successful applicant will be offered an appropriate appointment in the Radiation Oncology Department, University of Ottawa, and will be expected to participate in consultative and follow-up clinics.

There is a strong tradition of participation in clinical trials and clinical research within the Clinic and it is expected that the applicant will be willing to participate. He will be encouraged to develop his own clinic or laboratory research interests.

Applications with curriculum vitae and the names of three referees should be submitted to:
Dr. M. E. Tulloh, Director, Ontario Cancer Foundation, Ottawa Clinic, 190 Melrose Avenue, Ottawa, Ont.



Research & development

GUERBET

Better contrast media through research

Laboratoire GUERBET
16-24, rue Jean Chaptal - 93609 Aulnay-sous-Bois - Cedex FRANCE
Tél.: 929.78.37 - Télex: 212 382 F.

1981, *British Journal of Radiology*, *54*, 555–561
VOLUME 54 NUMBER 643

JULY 1981

The British Journal of Radiology

Diagnostic puncture in renal cystic dysplasia (multicystic kidney). Evidence on the aetiology of the cysts

By H. M. Saxton, F.R.C.P., F.R.C.R., *S. J. Golding, D.M.R.D., F.R.C.R.,
C. Chantler, M.A., M.D., F.R.C.P. and G. D. Haycock, M.B., B.Chir., M.R.C.P., D.C.H.

Departments of Radiology and Paediatric Nephrology, Guy's Hospital, London SE1 9RT

(*Received January 1981*)

ABSTRACT

Five cases of cystic dysplastic (multicystic) kidney occurring in infancy are described, in whom diagnostic puncture was used to confirm the suspected diagnosis. The characteristic finding on contrast injection was that the cystic spaces communicated via tubular structures, presumably nephronic, so ruling out the possibility of hydronephrosis. This finding also supports the view that cysts in multicystic kidney derive from nephrons and are not due to dilated calices. Although urography and ultrasonography both give appearances highly suggestive of multicystic kidney, the appearances on renal puncture are pathognomonic. When such appearances are demonstrated there is no urgent need for operative removal, except when necessitated by the size of the mass.

The cystic dysplastic kidney (multicystic kidney) is one of the most common causes of a unilateral mass and non-functioning kidney in the neonate. The diagnosis is usually reached by urography, which shows the absence of a normal kidney and which may show opacification in cyst walls—the "crescents" of Felson and Cussen (1975)—or late contrast opacification in the cysts—the "puddling" of Young *et al.* (1974). More recently, ultrasound has been employed both antenatally (Older *et al.*, 1979) and postnatally (Bearman *et al.*, 1976). Both these techniques give a strong indication of the likely nature of a non-visualized kidney but they seldom distinguish with complete certainty between cystic dysplastic kidney and severe neonatal hydronephrosis. Following our earlier experience of renal puncture in infancy (Saxton *et al.*, 1973), we have used renal puncture in five

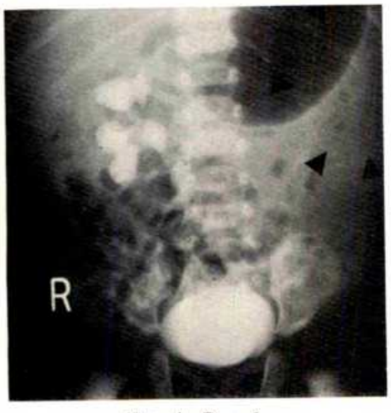


FIG. 1. *Case 1.*

Excretory urography. There is good concentration in the right kidney. No opacification is seen on the left but a curvilinear density is present (arrows) suggesting a cyst wall or stretched parenchyma.

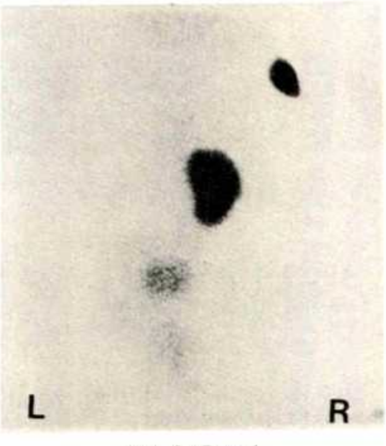


FIG. 2. *Case 1.*

DMSA scan. There is good uptake in a normal right kidney with no evidence of functioning renal tissue on the left.

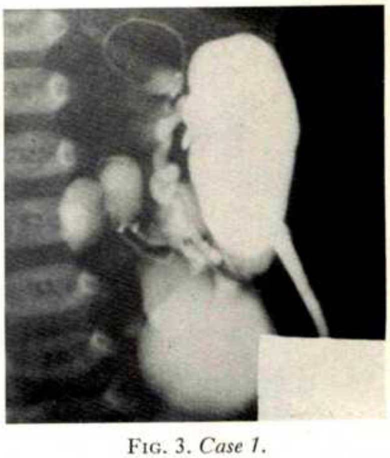


FIG. 3. *Case 1.*

Renal puncture. Contrast medium injected into the most lateral cyst superiorly flowed through the tubules on its medial aspect to enter the other cysts.

---

*Present address: The Royal Marsden Hospital, Sutton, Surrey.

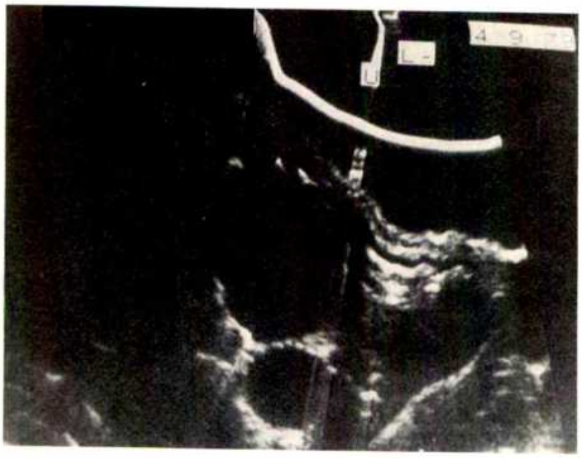


Fig. 4.

Fig. 4. *Case 2.*

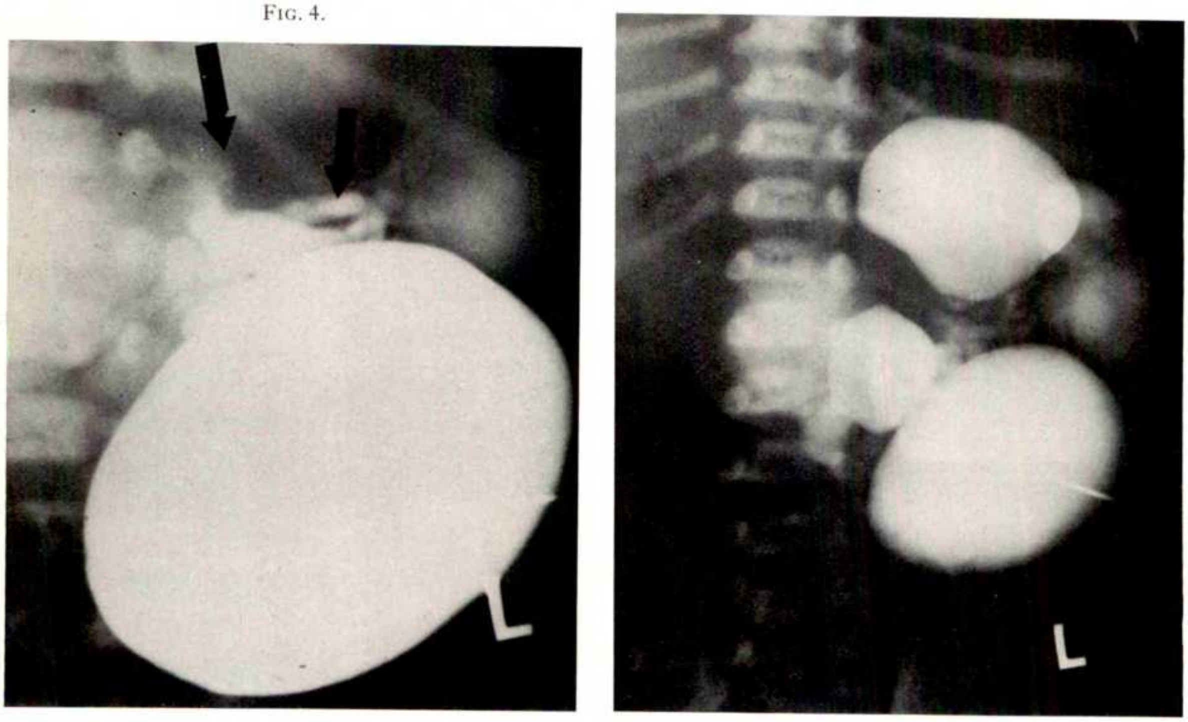
Longitudinal ultrasound scan of the abdomen. There are multiple transonic cysts in the left side, the largest cyst lying laterally.

Fig. 5. *Case 2.*

Renal puncture using an AL approach to the largest cyst.

(A) Initial injection opacified the cyst and outlined tubules on its cranial aspect (arrows).

(B) Further contrast showed the other cysts clustered around the centrally placed tubules.



A Fig. 5. B

such cases. The appearances are characteristic and, we believe, contribute to the understanding of the nature of the cystic dysplastic kidney.

Technique

The infant is strapped prone to a padded frame—light sedation is usually adequate. The dysplastic kidney is located on fluoroscopy by reference to the spine and lower ribs: we have not found it necessary to use ultrasonic localization during puncture although in Case 2 the fact that ultrasound had demonstrated a prominent cyst lying beneath the abdominal wall indicated that an antero-lateral (AL) approach was more appropriate.

A 3 cm fine (21 or 22 gauge) needle is passed through the skin under local anaesthesia and advanced until a respiratory swing is seen. Entry of a cyst is usually indicated by free back flow of clear fluid but gentle aspiration through a flexible connection may be required.

Contrast medium injection is then made under fluoroscopic control and several radiographs taken.

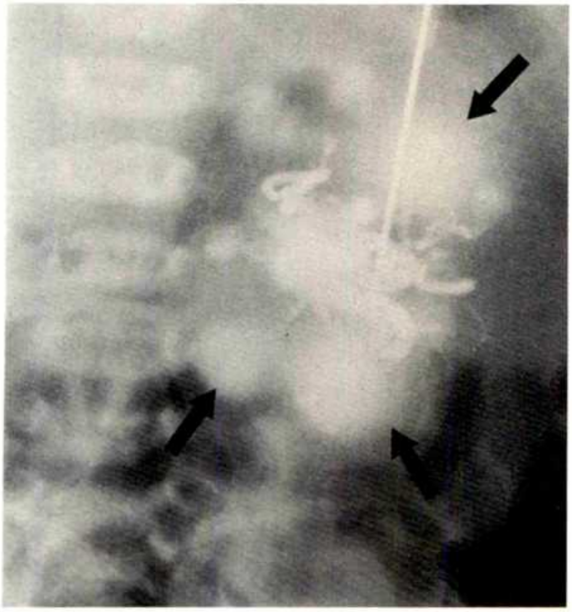


FIG. 6. *Case 3.*

Renal puncture. Contrast medium injected into a central cyst flowed through surrounding tubules to pool in other cysts (arrows).

Fluoroscopy and radiographs during the early stage of filling show opacification of tubular structures as discussed below.

There have been no sequelae to this procedure in our experience. In Case 2 the cysts were aspirated before removing the needle and in Case 5 a drainage catheter was inserted into the cysts for decompression prior to surgery.

CASE REPORTS

Case 1

A female child was born by normal delivery at 39 weeks following a pregnancy complicated by poor fetal growth. At birth she was small, with a birth weight below the tenth percentile, and had a left-sided tense abdominal mass. Serum creatinine and blood urea were normal.

Ultrasound showed a large multicystic lesion occupying the left side of the abdomen. On the right there was separation of the echoes from the renal sinus, suggesting mild hydronephrosis. IVU confirmed the presence of distended calices on the right but showed good transit of contrast into the bladder. On the left side a curvilinear density was seen suggesting a cyst wall or dilated calix (Fig. 1). Micturating cystography was normal. DMSA scan showed normal uptake of nuclide on the right and no evidence of functioning renal tissue on the left (Fig. 2).

Renal puncture and contrast medium injection showed a large cyst communicating with further cysts through tortuous tubules (Fig. 3).

No specific treatment was indicated and she was discharged on prophylactic antibiotics. Subsequent IVUs have shown infundibular narrowing of the upper pole calices on the right and stenosis of the right ureter at the pelvic brim with persistent caliceal dilatation. Her creatinine level has remained normal and she continues well although underweight for her age.

Case 2

A male child was delivered by elective lower segment Caesarian section at 38 weeks. Antenatal ultrasound at 30 and 38 weeks had demonstrated a multicystic abdominal mass. At birth there was an obvious mass in the left side of the abdomen but no other abnormal findings.

IVU showed normal appearances on the right and no opacification on the left. Ultrasound examination confirmed the presence of a multicystic space-occupying lesion on the left side (Fig. 4).

Renal puncture was carried out by a left AL approach to the prominent cyst demonstrated by ultrasound. Initial filling of this cyst showed tubules lying on its cranial aspect (Fig. 5A) and on further injection contrast medium passed slowly into surrounding cysts (Fig. 5B) until the whole area was filled. From the cyst 75 ml of aspirate were withdrawn, at which point it became impalpable.

Six months after birth the child was well. The fluid had reaccumulated and the kidney was readily palpable. One year after birth he remains well and the kidney is impalpable.

Case 3

A female child was born at term after a normal pregnancy. On examination, there was a tense mass in the left loin. Serum creatinine and blood urea were normal.

IVU was normal on the right with no opacification on the left. Micturating cystography revealed mild reflux into the distal right ureter.

Renal puncture showed filling of a cystic space communicating with tortuous tubules (Fig. 6). Further injection of contrast medium filled other cysts in the left loin through these tubules, demonstrating a large multicystic kidney. There was no filling of pelvis or ureter. There were no complications and the child remained well ten months after birth.

Case 4

A female child was born by elective forceps delivery after spontaneous rupture of the membranes at 35 weeks gestation. Antenatal ultrasound had shown a collection of cysts within the abdomen (Fig 7). At birth the child appeared normal apart from a smooth firm mass in the right loin. Serum creatinine was elevated to 141 μmol/l. IVU showed no appreciable accumulation of contrast medium in either kidney but a curvilinear density on the right (Fig. 8), suggesting the wall of a dilated calix or cyst. Ultrasound confirmed the presence of a multicystic lesion on the right but the left kidney was not demonstrated. Micturating cystography was normal. DMSA renal scan showed no significant uptake on the right but moderate uptake in an irregular, low-lying left kidney and DPTA dynamic renal scan showed good excretion from this kidney (Fig. 9).

Renal puncture initially filled one small cyst communicating through several large tortuous tubules to fill the other cysts throughout the renal area (Fig. 10).

The creatinine level fell to normal during the few weeks after delivery and no active treatment was required. Six months after delivery the child remains well.

Case 5

A female child was delivered at 35 weeks gestation by Caesarian section following fetal distress. At birth there was marked abdominal distension and an IVU showed a normal right kidney with non-opacification on the left (Fig. 11). Micturating cystography was normal. Ultrasound demonstrated a multilocular cystic lesion occupying most of the abdomen. The left kidney was not identified. A barium meal showed cranial displacement and compression of the second part of the duodenum (Fig. 12), and displacement of the rest of the gut to the outer limits of the abdomen around the mass. A DMSA scan showed a normal right kidney with no uptake on the left side.

Renal puncture initially filled one large tubule through which contrast medium passed to fill a large multilocular

P 25, 824.

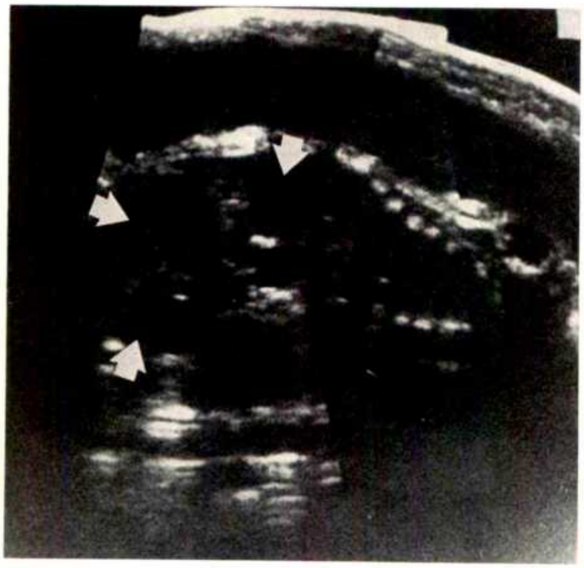


FIG. 7. *Case 4.*
Antenatal ultrasound. Longitudinal scan of the fetus showing the fetal ribs and spine on the right of the image. The abdomen is occupied by multiple transonic cysts (arrows).

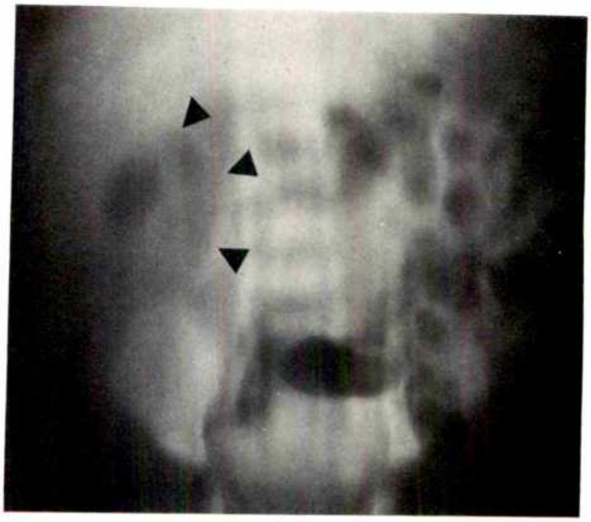


FIG. 8. *Case 4.*
Excretory urography. Tomography 15 minutes after injection shows no normal opacification of either kidney. On the right is a curvilinear density suggesting a cyst wall or dilated calix (arrows).

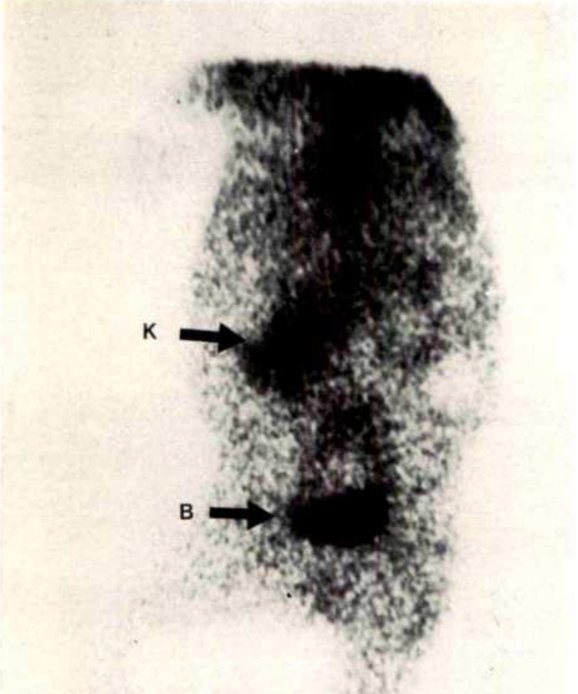


FIG. 9. *Case 4.*
DTPA scan showing good uptake in an irregular low-lying kidney (K) and good excretion into the bladder (B). There is no uptake in the region of the right kidney.

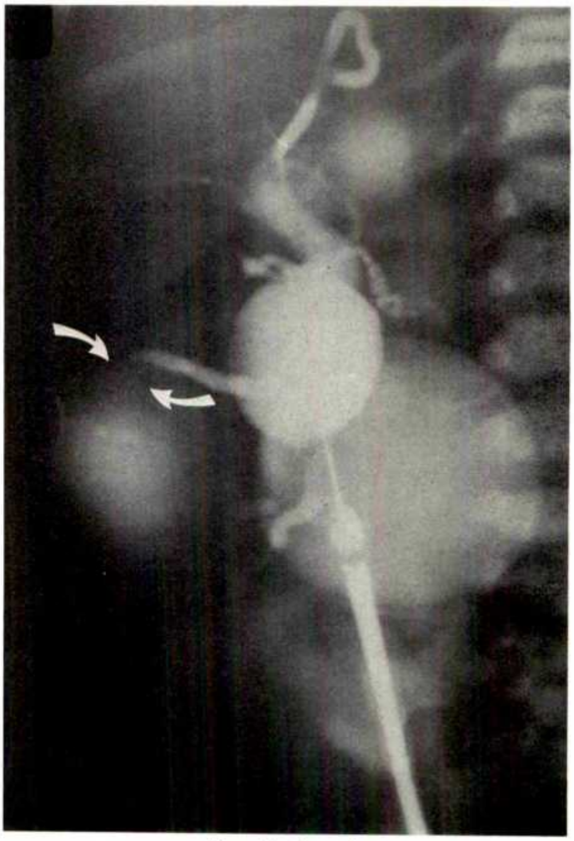


FIG. 10. *Case 4.*
Renal puncture. Contrast medium injected into a central cyst passed through several tubules to collect in other cysts. Contrast can be seen flowing from one tubule (arrows) to pool in a cyst.

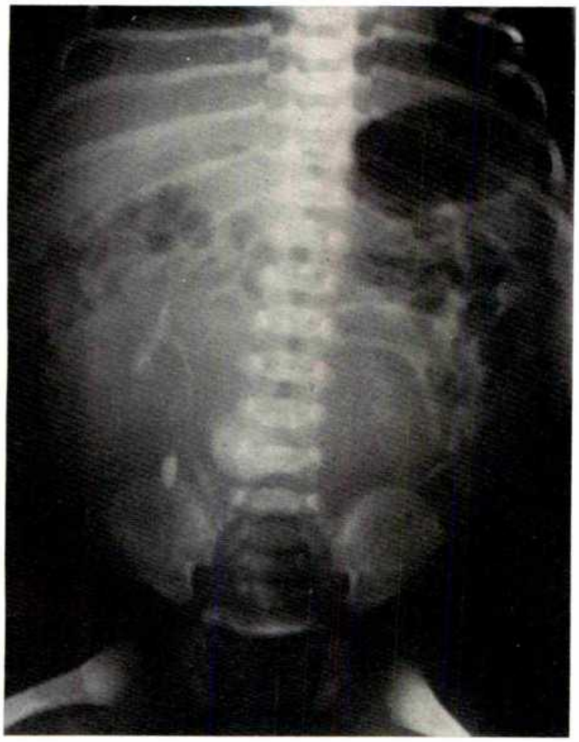


FIG. 11. *Case 5.*

Excretory urography. There is a normal right kidney but no opacification on the left. There is a central mass displacing the bowel gas outwards and compressing the bladder from above.

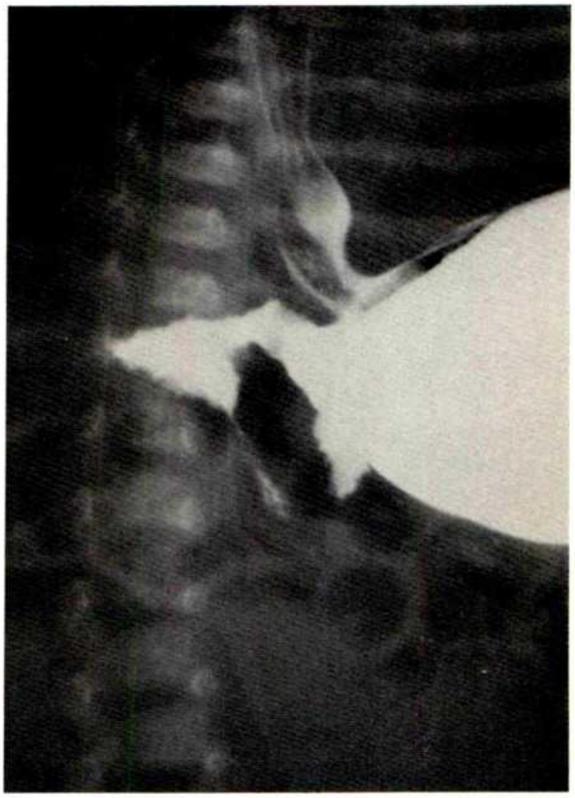
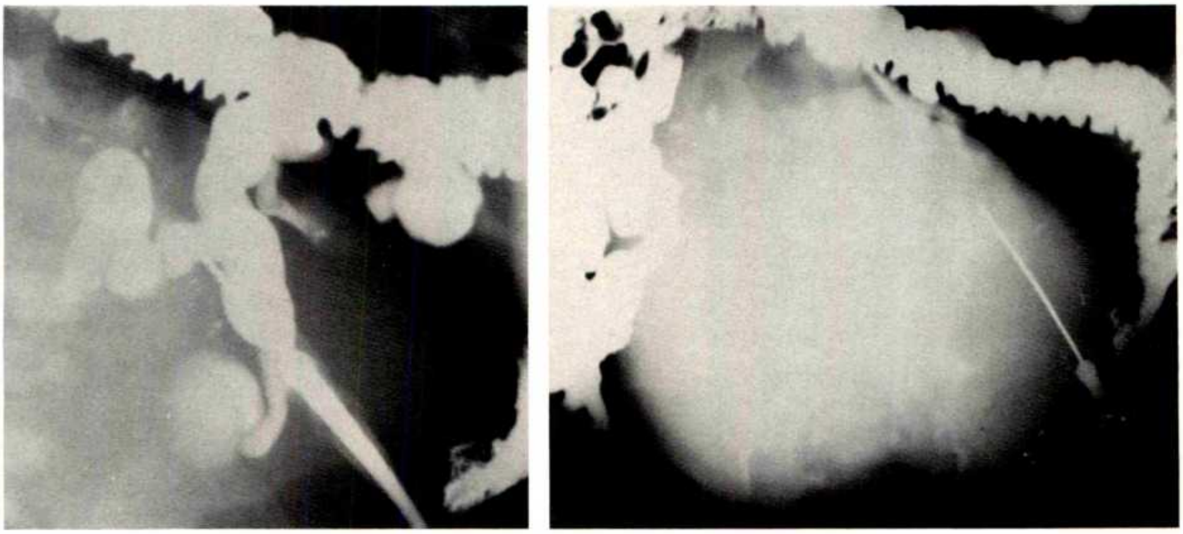


FIG. 12. *Case 5.*

Barium meal. A right anterior oblique view shows upward displacement and stretching of the second part of the duodenum with delay in gastric emptying.



A FIG. 13. *Case 5.* B

Renal puncture.

(A) The needle entered a large tubule and contrast medium flowed into surrounding cysts. The barium-filled colon is displaced superiorly.

(B) Further filling opacified a large cyst occupying the pelvis and displacing the bowel.

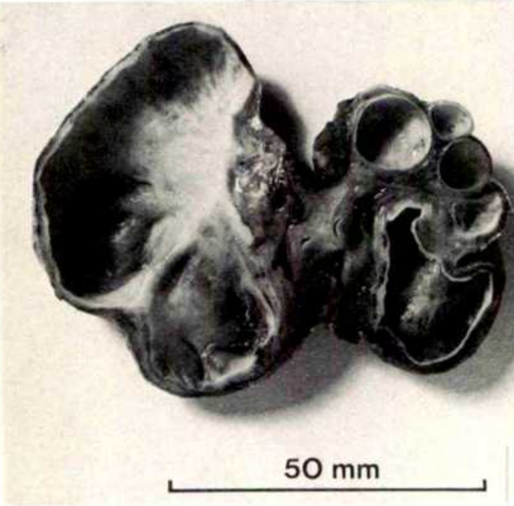


FIG. 14. *Case 5.*

Multicystic kidney removed after percutaneous decompression. The cut surface of the specimen shows the relationship of the cysts to the central area containing tubules through which the cysts communicate.

cyst occupying most of the abdomen and extending into the pelvis (Fig. 13). In view of the presence of duodenal compression a percutaneous catheter was inserted posteriorly to drain the cysts prior to surgery.

At operation the left proximal ureter was atretic, no left renal pelvis could be found and a collapsed multicystic kidney was removed with ease from the left renal fossa. Examination of the specimen showed a central core of tissue surrounded by numerous large cysts (Fig. 14). The central area was occupied by small cysts and tubules and fluid could be squeezed from one cyst to another through this area. Histology of this part revealed cysts and tubules of all sizes in a framework of dysplastic fibrous tissue, characteristic of renal dysplasia. She made a good recovery and two months after surgery continues well.

DISCUSSION

Aetiology of renal cystic dysplasia

Renal cystic dysplasia is generally accepted as being due to ureteric atresia, with absence of the renal pelvis and failure of normal nephrogenesis (Griscom *et al.*, 1975). Felson and Cussen (1975) however, regard the cysts as dilated calices and believe that the multicystic kidney is simply an extreme form of hydronephrosis. Their belief is based on three findings. First is the occurrence of opacification on the margins of cysts after intravenous contrast medium, which they compare to the crescents described by Dunbar and Nogrady (1970) in cases of marked hydronephrosis. Second, they regard the opacification of cysts due to contrast appearing in them (Young *et al.*, 1974; Cooperman, 1976) as indicating that the cysts are really calices. Third, the fact that cysts may intercommunicate (Felson and Cussen, 1975) might also appear to bear out this theory.

The "crescents" seen in their cases and in some of our material are not strictly analogous to those described by Dunbar and Nogrady (1970). These authors describe limited areas of crescentic opacification in the caliceal regions of obstructed kidneys with relatively normal parenchyma lying peripherally. The opaque areas in multicystic kidneys are rings around the cysts and are not limited to one part. In our view, they indicate only that there are some functioning glomeruli and nephrons and that contrast medium is appearing in them. When such nephrons are present, they will be best visualized where they are projected "edge-on" to the X-ray beam: clearly this would be around the margins of a cyst or cysts. Such areas represent strands of nephron-containing tissue and cannot be adduced as evidence for or against hydronephrosis.

The opacification of cysts also carries no aetiological implications, since it is known that cysts in adult and infantile polycystic disease are connected dynamically to patent nephrons (Bricker and Patton, 1955). It is also well known that sufficient contrast medium may be excreted into simple cysts after intravenous injection to increase the attenuation coefficient of the cyst when examined by CT scanning.

The passage of fluid between cysts is readily explained by the presence of communicating tubules which we have demonstrated. X-ray studies on the kidney after removal might well fail to show these tubules, unless films were taken during or soon after injection of contrast medium; shortly after the injection is ended the tubules have ceased to be opaque in our cases. Nevertheless, Fig. 5C of Felson and Cussen's paper shows appearances strongly suggesting such tubules.

There is a striking similarity between our pictures and the diagramatic representation of renal cystic dysplasia given by Potter (1972) (Fig. 15). The presence of tubules terminating in cysts is also borne out by microdissection studies (Madewell *et al.*, 1979). We believe that our evidence gives weight to the belief that such cysts arise from nephrons obstructed during development, usually because of ureteric atresia.

Value of diagnostic puncture

As we have already noted, the diagnosis of renal cystic dysplasia can often be made with reasonable certainty on urography or ultrasound. As a preliminary to removal of the kidney these are quite sufficient. However, it may not be possible by these

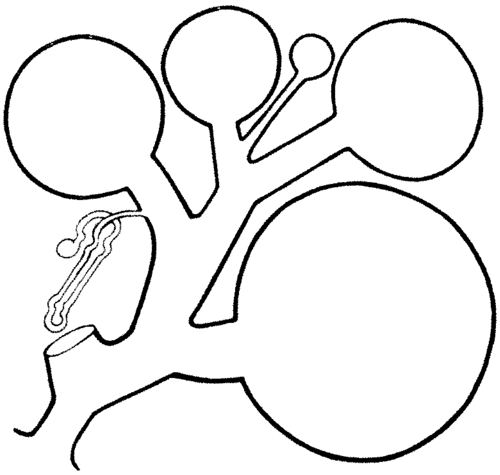


FIG. 15.
Diagrammatic representation of renal cystic dysplasia showing branching tubules which terminate in cysts and are connected to some normal nephrons. (Reproduced with permission from Potter, 1972).

methods to distinguish with certainty between cystic dysplasia and severe unilateral hydronephrosis, and if surgery is to be deferred until a more suitable age there is some value in achieving a positive distinction between these two conditions. Multicystic kidney requires no immediate treatment except where the mass effect is a problem, as in our Case 5. However, in view of the suggestion that cystic dysplasia may cause hypertension (Javadpour *et al.*, 1970), many clinicians would probably prefer the kidney to be removed eventually.

Infection, which may occur in neonatal hydronephrosis, is at present presumed unlikely where there is ureteric atresia. We believe that there are therefore advantages in using renal puncture as an ultimate arbiter in cases of doubt. The absence of a collecting system is suggestive, and the opacification of tubules is, we believe, pathognomonic of cystic dysplasia. In Case 5 the cysts were so large that it was impossible to be sure that there was no renal pelvis and only the opacification of tubules on puncture made it possible to distinguish this from hydronephrosis.

Other aspects of cystic dysplasia

Only one of our cases, Case 1, showed the changes in the opposite kidney which have been described by other authors (Greene *et al.*, 1971; Newman *et al.*, 1972). In Case 4 the contralateral kidney did not opacify at urography and the nature of the pathology in this kidney has not been determined but in view of the fact that the kidney showed good uptake of DMSA and has maintained good function, no further investigations were carried out in the neonatal period. None of the three cases we investigated with isotope scans showed any significant uptake of nuclide in the dysplastic kidney, probably owing to the relatively small number of normal nephrons in these kidneys.

ACKNOWLEDGMENTS

We are grateful to our colleagues Mr. D. Drake, Mr. M. Joyce and Mr. H. Kinder for advice of the surgical management of these patients, to Dr. B. King and Dr. A. Saunders for the ultrasound and Dr. M. Maisey for the isotope examinations, and to Dr. D. Turner for advice on the histology. The illustrations were prepared by the Departments of Medical Photography of the Royal Marsden and Guy's Hospitals.

REFERENCES

BEARMAN, S. B., HIAE, P.L. and SANDERS, R. C., 1976. Multicystic kidney; a sonographic pattern. *Radiology, 118*, 685–688.

BRICKER, N. S. and PATTON, J. F., 1955. Cystic disease of the kidneys: a study of dynamics and chemical composition of cyst fluid. *American Journal of Medicine, 18*, 207–219.

COOPERMAN, L. R., 1976. Delayed opacification in a congenital multicystic kidney. *Radiology, 121*, 703–705

DUNBAR, J. S. and NOGRADY, M. B., 1970. The caliceal crescent — a roentgenographic sign of obstructive hydronephrosis. *American Journal of Roentgenology, 110*, 520–528.

FELSON, B. and CUSSEN, L. J., 1975. The hydronephrotic type of unilateral congenital multicystic disease of the kidney. *Seminars in Roentgenology, 10*, 113–123.

GREENE, L. F., FENZAIG, W. and DAHLIN, D. C., 1971. Multicystic dysplasia of the kidney with special reference to the contralateral kidney. *Journal of Urology, 105*, 482–487.

GRISCOM, N. T., VANTER, G. F. and FELLERS, F. X., 1975. Pelvoinfundibular atresia—the usual form of multicystic kidney. *Seminars in Roentgenology, 10*, 125–131.

JAVADPOUR, N., CHELOUHY, E. and MONCADO, L., 1970. Hypertension in a child caused by multicystic kidney. *Journal of Urology, 104*, 918–921.

MADEWELL, J. E., HARTMAN, D. S. and LICHTENSTEIN, J. E., 1979. Radiologic-pathologic correlation in cystic disease of the kidney. *Radiologic Clinics of North America, 17*, 261–279.

NEWMAN, L., SIMMS, K., KISSANE, J. and MCALISTER, W. H., 1972. Unilateral total renal dysplasia in children. *American Journal of Roentgenology, 116*, 778–783.

OLDER, R. A., HINMAN, C. G., CRANE, L. M., CLEEVE, D. M. and MORGAN, C. L., 1979. In utero diagnosis of multicystic kidney by gray scale ultrasonography. *American Journal of Roentgenology, 131*, 130–1.

POTTER, E. L., 1972. *Normal and Abnormal Development of the Kidney* (Year Book Medical Publishers, Chicago), p. 154.

SAXTON, H. M., CAMERON, J. S., CHANTLER, C. and OGG, C. S., 1973. Renal puncture in infancy. *British Medical Journal, iii*, 267–270.

YOUNG, L. W., WOOD, B. P., SPOHR, C. H. and PANNER, B., 1974. Delayed excretory urographic opacification—a puddling effect, in multicystic renal dysplasia. *Annales de Radiologie*, (Paris), *17*, 391–396.

1981, *British Journal of Radiology*, *54*, 562–565

The radiology of Meconium Ileus Equivalent

By D. W. Pilling, M.B., D.C.H., F.R.C.R.
Alder Hey Children's Hospital, Liverpool
and G. M. Steiner, M.B., F.R.C.P., F.R.C.R.
Children's Hospital, Sheffield

(*Received January 1981*)

Abstract

Meconium Ileus Equivalent is a condition which occurs in patients with cystic fibrosis where the ileum becomes obstructed by bowel content of abnormal consistency. Intercurrent chest infection or absence of pancreatic extract supplements are often the exacerbating cause. Plain films of the abdomen show small bowel obstruction and in some a nodular pattern in the small bowel, the nodules being larger than those seen in quiescent cystic fibrosis. Gastrografin enemas and/or enemas with acetyl cysteine can be used in the treatment of the condition, the Gastrografin having the advantage of confirming the diagnosis radiologically.

The condition is important as it can be the presenting feature of cystic fibrosis in childhood and even in early adult life, and the operative mortality and morbidity are high. Conservative treatment should be pursued vigorously and operation only undertaken if unavoidable.

Meconium Ileus Equivalent was first described by Rasor and Stevenson (1941) and strictly speaking is limited to obstruction of the terminal ileum by "putty"-like material; but the diagnosis is often applied to patients with cystic fibrosis also, who have abnormal intestinal contents, partially or completely obstructing the small bowel. This condition is probably becoming commoner due to increased survival of patients as a result of more intensive therapy of chest infections.

Whilst most of the patients presenting with this condition are children with known cystic fibrosis, the condition has been described as the presenting feature of cystic fibrosis in adults. This paper describes four children who developed Meconium Ileus Equivalent, two as a presenting feature of the condition, one who developed the condition ten years after the initial presentation with Meconium Ileus in the neonatal period and one for whom this was a complication of the already diagnosed cystic fibrosis.

Case 1

This patient presented at five days of age with a history of vomiting every feed but no bile and not passing meconium. A rectal wash-out had produced a thin mucus plug. The abdomen was distended and a plain film showed evidence of small bowel obstruction. At laparotomy the appearances were shown to be those of Meconium Ileus with the terminal ileum obstructed by abnormal bowel content and the ileum proximal to this was brought out as an ileostomy. Oral pancreatic enzyme was started. The ileostomy was closed at four months of age. The patient had repeated chest infections but no further bowel upset until ten years of age, when he presented with abdominal pain, and a mass in the right iliac fossa, and plain films of the abdomen showed small bowel obstruction with a faecal mass in the right side of the abdomen. The patient was treated with oral Pancrex and Gastrografin enemas. Figure 1 shows Gastrografin study of the terminal ileum with thickened folds and nodules in the terminal ileum. After three days with increasing abdominal distension, a laparotomy showed adhesions and obstruction of the terminal ileum by faecal material. An ileostomy was fashioned and wash-outs of the bowel through the ileostomy were performed over a period of several days. After a stormy post-operative course, including the development of a pelvic abscess, the ileostomy was eventually closed and the patient has had no recurrence of the abdominal sysmptoms since his Pancrex dose was increased. Whilst there was no history of reduction of Pancrex prior to the obstruction, decrease in relative dose due to growth of child may have contributed to the intestinal obstruction.

Case 2

This patient presented at four years old because of failure to thrive. No cause was found. The sweat test at this time was reported normal, but a repeat was suggested for technical reasons. Before this repeat has been carried out she

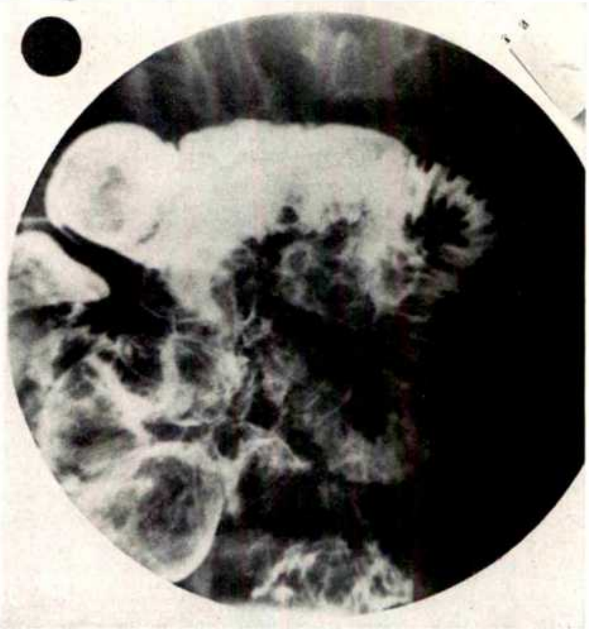


Fig. 1.

Gastrografin study of the distal small bowel through a double-barrelled ileostomy showing coarse mucosal folds in the ileum and abnormal bowel content distending the ileum.

presented with abdominal pain and abdominal distension. On examination a mass was palpable in the right iliac fossa and there was visible peristalsis. A plain abdominal radiograph (Fig. 2) showed faeces in the large bowel and a mass in the right iliac fossa with small bowel obstruction. Coarse nodular shadowing in the gas-filled bowel, in the left upper quadrant, was also seen. Gastrografin enemas and oral acetyl cysteine were administered which relieved the obstruction and there has been no recurrence of the abdominal symptoms. A repeat sweat test showed an elevated sodium level, diagnostic of cystic fibrosis.

Case 3

This patient presented at age 11 and was known to have had cystic fibrosis since the age of three. She had been taking Pancrex orally since diagnosis, and there was no history of recent change in the dose. She presented with a mass in the right iliac fossa and abdominal distension of several months' duration. Investigation by a general surgical team had included barium meal and follow-through and barium enemas, and diagnoses of tuberculosis, Crohn's disease and appendix abscess were all considered. In view of her known cystic fibrosis the diagnosis of Meconium Ileus Equivalent was thought to be more likely, and she was treated with acetyl cysteine enemas and oral acetyl cysteine, which resolved the abdominal mass. This mass has since recurred on several occasions but on each occasion has responded to increased oral acetyl cysteine.

Case 4

This patient had presented at the age of two years and six months with recurrent rectal prolapse and failure to thrive. During the investigation she developed bile-stained vomiting, constipation and abdominal distension. A plain film of the abdomen at this stage (Fig. 3) showed obstruction of the small intestine and a faecal mass in the right iliac fossa. There were also coarse nodules in the bowel in the left hypochondrium. At laparotomy the following day the terminal ileum was found to be obstructed by faecal material. These contents were expressed into the colon manually and Gastrografin was instilled via the rectum into the colon at operation. Her bowel actions returned to normal in five days but she developed a severe chest infection and over the following six weeks deteriorated and died.

DISCUSSION

The plain film changes in these patients show a bubbly, granular appearance, predominantly in the right side of the abdomen, with dilated small bowel and fluid levels due to small bowel obstruction.

Two patients quite clearly showed coarse, nodular shadows attached to the mucosa in the left hypochondrium. The cause of these is uncertain, but they

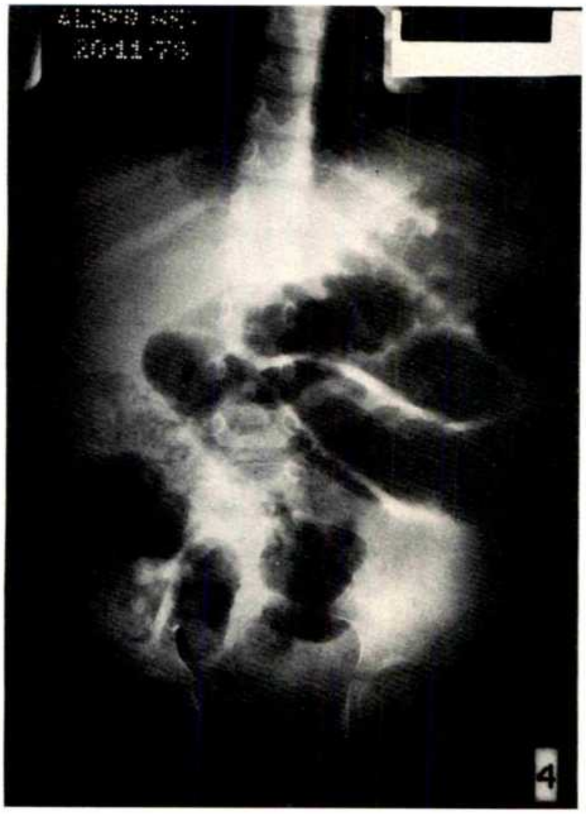


FIG. 2.

Supine abdomen showing dilated small bowel due to obstruction. Note the nodules in the bowel in the left hypochondrium and the faecal mass in the right lower abdomen.

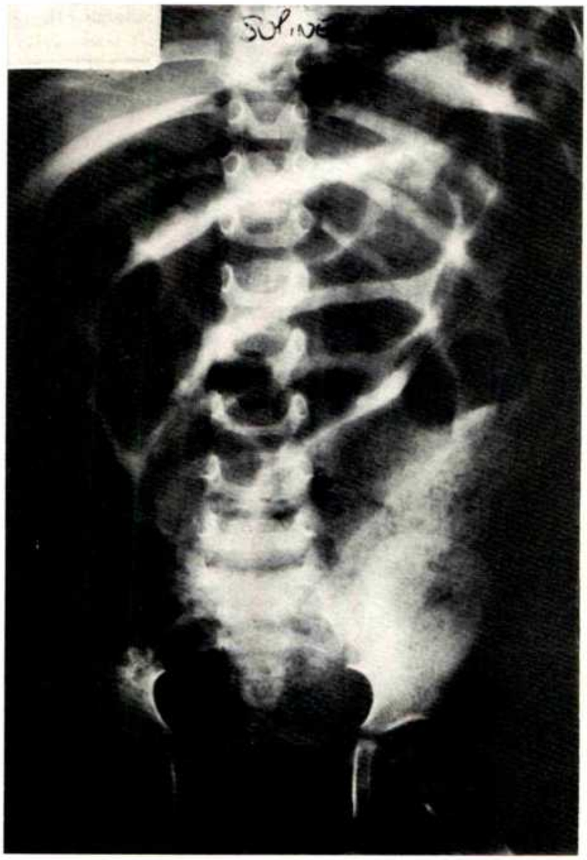


FIG. 3.

Supine abdomen showing a faecal mass in the lower abdomen and small bowel obstruction.

almost certainly lie in the small bowel, as the large bowel at this site is full of faeces rather than gas in these patients. They may represent the coarse mucosal pattern described in the jejunum exaggerated by the presence of intestinal obstruction. They appear so large that it seems unlikely that they represent the dilated goblet cells thought to be the cause of the small nodules seen in quiescent cystic fibrosis (Bartram and Small, 1971). Although only seen in two patients, it may be that the nodular appearance in the proximal small bowel is a helpful sign of Meconium Ileus Equivalent.

For confirmation of the diagnosis a contrast enema is the method of choice. Gastrografin is preferred to barium as it not only confirms the diagnosis but may help to relieve the obstruction by drawing water into the lumen of the bowel and by its action as a wetting agent. The enema can be repeated several times until obstruction is relieved. A contrast enema will also be helpful in excluding the other possible causes of these symptoms, including intussusception, itself a well-known complication of cystic fibrosis (Caffey, 1979). Cases have been described in which these two conditions co-existed (Snyder and Gwinn, 1964). The enema may also demonstrate the nodular changes of cystic fibrosis in the large bowel. Weinstein *et al.* (1968) reviewed a series of patients with Meconium Ileus Equivalent; only 57% of their series had classical large bowel appearances of redundant folds and marginal filling defects. Under the age of five, this was only 11% which may explain the lack of large bowel lesions seen on contrast enemas in our cases where two of the patients were under the age of five. Thirty-eight per cent of Weinstein's series had abnormal small bowel appearances, and this was not age-related. Only one of our patients had an adequate demonstration of the small bowel, which showed thickened folds with small nodules, as described by other authors.

A contrast meal is not usually helpful in the acute phase, and the use of barium is absolutely contra-indicated as it will only aggravate the obstruction without providing any relevant information. The importance of making the diagnosis early and instituting treatment with oral acetyl cysteine or acetyl cysteine and/or Gastrografin enemas is exemplified by Case 1, for whom surgery was necessary because obstruction was not relieved by Gastrografin enemas, and Case 4 who was operated upon without prior enema. Following surgery they had very stormy and lengthy post-operative courses, and the fourth patient died of chest complications. This is in keeping with the experience of others (Hodson *et al.*, 1976), who reported three patients who needed operation, of whom one died and the other two had serious post-operative complications.

Several factors are thought to trigger-off Meconium Ileus Equivalent. Most commonly an intercurrent chest infection or stopping of the oral pancreatic enzyme supplement are implicated (Fisher, 1954). These will affect the consistency of the bowel content and cause obstruction. The obstruction most commonly occurs in the terminal ileum where circular folds are deficient and where, even in normal patients, the small bowel content is at its most solid (Garnham and Carter, 1964). Two of our cases were not receiving oral pancreatic enzyme, and this probably explains their presentation. In one of the others there is some evidence that the dose of pancreatic supplement he was receiving prior to obstruction had not been sufficiently increased as he grew in size. The cause in the remaining case is obscure. At first sight it would seem unusual that Meconium Ileus Equivalent occurs so rarely in patients who have had Meconium Ileus in the neonatal period, our Case 1 being one of very few described in the literature. This is not because the prognosis of the chest complications of patients presenting earlier with Meconium Ileus is any worse, but probably because the aetiologies of Meconium Ileus Equivalent and Meconium Ileus are different. It has been shown (Thomaidis and Arey, 1963) that there are severe changes in the mucous glands of the bowel in Meconium Ileus, with pancreatic function playing little if any part. In contrast, Meconium Ileus Equivalent is thought to be related much more to abnormality of pancreatic enzymes. This is borne out by the frequent history of cessation of pancreatic extract supplements immediately prior to the development of Meconium Ileus Equivalent.

The condition is relatively uncommon but it is important that it is recognized for several reasons. These are:

(1) It is a potentially lethal complication of cystic fibrosis.

(2) The operative mortality and morbidity are very high.

(3) As cystic fibrosis patients are surviving longer, the condition will present beyond the paediatric age range; also, in adults the sweat test is unreliable for the diagnosis of cystic fibrosis, and a negative test does not rule out the condition (Weinstein *et al.*, 1968).

REFERENCES

BARTRAM, C. I. and SMALL, E., 1971. The intestinal radiological changes in older people with pancreatic cystic fibrosis. *British Journal of Radiology*, *44*, 194–197.

CAFFEY, J., 1979. *Pediatric X-ray Diagnosis*. 8th Edit. (Year Book Medical Publications, Chicago), p. 749.

FISHER, O. D., 1954. Intestinal obstruction as a late complication of fibrocystic disease of the pancreas. *Archives of Disease in Childhood, 29,* 262–264.

GARNHAM, J. R. and CARTER, T. R. G., 1964. Mechanical intestinal obstruction in a young adult male with mucoviscidosis. *Gut, 5,* 256–259.

HODSON, M. E., MEARS, M. B. and BATTEN, J. C., 1976. Meconium Ileus Equivalent in adults with cystic fibrosis of the pancreas. A report of six cases. *British Medical Journal, 2 (2)*), 790–791.

RASOR, G. B. and STEVENSON, W. L., 1941. Meconium Ileus Equivalent. *Rocky Mountain Medical Journal, 38,* 218–220.

SNYDER, W. H. and GWINN, J. L., 1964. Fecal retention in children with cystic fibrosis. *Pediatrics, 34,* 72–77.

THOMAIDIS, T. S. and AREY, J. B., 1963. Intestinal lesions in cystic fibrosis of the pancreas. *Journal of Pediatrics, 63,* 444.

WEINSTEIN, L. D., CLEMETT, A. R. and HERSKOVIC, T., 1968. Morphologic and radiologic findings in the intestines in cystic fibrosis. *Gastroenterology, 54,* 1282.

Book review

A Textbook of Radiology and Imaging. Ed. by David Sutton, 3rd edit., pp. xv+1140+Index, 1980 (Churchill Livingstone, Edinburgh), £65·00.
ISBN 0443–01700X

The first edition of this British textbook was published in 1969. A second edition appeared in 1975 and now a much awaited third edition has been published. There are seven sections as before, with three new contributors and a new section on non-radiological imaging of six chapters with seven contributors. Accordingly, the title has been changed to include imaging, there is a larger page size and it may now be purchased as a single volume or as two volumes. Diagnostic imaging has become more wide-ranging during the last five years and Dr. Sutton and his co-authors have attempted to bring together all branches of the subject into one book.

A book of such size and scope presents certain problems to the reviewer. Firstly, there is an acute awareness that no one reviewer can do justice properly to so many different topics and he may well concentrate more critically on those which are of particular personal interest. Secondly, as this is the standard textbook of British radiology used by students preparing for higher qualifications, there is a responsibility to assess its value in this role.

The revised first seven parts remain a mine of valuable information which in the main is accurate, although there are some errors which can be attributed to lapses in proof reading. In general terms it is authoritative, comprehensive and precise, although some chapters do not reach as high a standard of content, balance and clarity as others. Despite the claim by the publishers that the new edition has been completely revised and brought up to date, this is not entirely true throughout the book. The new contributions on skeletal disorders of metabolic and endocrine disease, embryology and anatomy of the heart, congenital heart disease and mammography are excellent. Although the chapters on bone and joint disease remain good, there is nothing really new. For example, fuller descriptions of joint prostheses and their associated problems would have been welcomed. Again, in the chapters on chest disease the little used bronchial arteriography is illustrated, but there is no full description of the technical aspects or the anatomical and pathological considerations of mediastinal and lung tomography. Such examinations are performed daily in most X-ray departments. There are new illustrations but there are also old ones, some of which are of doubtful quality, and others repeated in the present edition have been reduced in size with some loss of information. Once again, too often there is the distracting separation of an appropriate illustration from the text, and small errors present in the 2nd edition have been repeated. Such criticism would be unnecessary if a little more care had been taken by the publishers.

Perhaps the main question to be answered is whether the addition of a separate new part on imaging to a revised 2nd edition has been successful. The authors and publishers must have been faced with the dilemma of publishing in the present format or delaying publication in order to produce a completely new textbook of integrated diagnostic imaging. It was presumably a decision taken with regard to time and timing. The six new chapters are excellent. The contributors are experts in their own particular fields and the reader is given basic information on the technical aspects of the investigations followed by a comprehensive account of their role and value in clinical diagnosis and patient management. All these chapters are illustrated to a high standard. However, the present format does not really work.

When reading the first seven parts of the book, time and time again one asks the question—What would be the role of ultrasound, radioisotope scanning and computerized tomography in the diagnosis of this or that tumour or disease process? In most chapters this information can only be obtained by repeated reference to the end of the book or even the companion volume. At best, this can be irritating and is frequently frustrating. Some contributors have, however, successfully managed to integrate the newer techniques into their texts. Echocardiograms, for instance, are included in the excellent chapters on the embryology of the heart and congenital heart disease. The five chapters on acquired heart disease would have gained by including echocardiograms. Ultrasound is introduced into the chapter on the acute abdomen but inexplicably there is no real mention of ultrasound or radioisotope scanning in the chapter on the biliary tract, particularly in that section on the investigation of jaundice. Similarly, the otherwise good chapters on the urinary tract undoubtedly suffer by not including the role of these new imaging techniques in clinical problem solving; for example, in renal failure, diagnosing space-occupying lesions etc.

Every reviewer feels a responsibility to make such comments, particularly about a book which presents British radiology to the English-speaking world. Nevertheless, it is a good book providing most of the essential information for a sound framework of radiological knowledge. It is well worth owning and should be made available in training departments of diagnostic imaging.

JOHN WILLIAMS.

1981, *British Journal of Radiology*, *54*, 566–571

The reliability of radiology in detecting prolactin-secreting pituitary microadenomas

By E. Teasdale, M.R.C.P., D.M.R.D., P. Macpherson, F.R.C.R., D.T.C.D. and
G. Teasdale, M.R.C.P., F.R.C.S.

Departments of Neuroradiology and Neurosurgery, Institute of Neurological Sciences
Southern General Hospital, Glasgow G51 4FT

(*Received December 1980*)

ABSTRACT

Radiological findings in 30 patients with proven prolactin-secreting pituitary adenomas, originally diagnosed exclusively by endocrine criteria, have been reviewed. Conventional tomography was the examination most often abnormal (50%), and changes or lack of changes corresponded to the state of the pituitary fossa as noted at operation in 93%. Tomographic abnormalities indicated the site of the tumour in 86%. Plain films were less sensitive (27% abnormal) although the changes reported were all confirmed during the surgical procedures. Although cavernous sinography and CT rarely yielded positive information unless either plain films or tomograms were abnormal, each may have a place in the assessment of a patient before operation: sinography to ensure that there is no significant anomaly of the carotid artery at the level of the pituitary fossa; CT scan to exclude a hypothalamic lesion or to detect an associated suprasellar tumour extension or intrasellar cisternal herniation. Strategies for the radiological investigation of patients suspected of having a prolactin-secreting pituitary tumour are proposed.

Only a proportion of patients with amenorrhoea, infertility, galactorrhoea and hyperprolactinaemia have an adenoma within the pituitary gland. Even after cases secondary to drugs or such disorders as hypothyroidism, renal failure or hypothalamic-pituitary stalk lesions have been excluded, the source of the elevated prolactin may be a diffuse abnormality of the control of pituitary secretion, and not a discrete tumour. This distinction is important because, although medical treatment is available for all forms of hyperprolactinaemia, operation is appropriate only in cases with tumours. Conventionally, detection of a tumour, and therefore selection of patients for operative treatment, depends upon radiological methods such as plain radiology, conventional and computed tomography and cavernous sinography. Because of this it has usually been possible to compare surgical and radiological findings only in patients considered to have abnormal results. We had the unusual opportunity to study a series of patients with prolactin-secreting pituitary adenomas who were selected for surgery purely on the basis of endocrine criteria, irrespective of the presence or absence of radiological abnormality. This has enabled us to assess the accuracy of radiological techniques and their usefulness in the investigation of this disorder.

PATIENTS AND METHODS

Radiological studies were performed on 30 women with hyperprolactinaemia who were considered, on the basis of clinical and endocrine features reported previously (Cowden *et al.*, 1979) as being likely to have a prolactinoma. No patient had clinical evidence of visual field impairment. Each patient was studied by plain radiology, tomography, cavernous sinography and computed tomography (CT).

Lateral and frontal skull views were taken. Tomographic cuts of 1.4 mm thickness were made at 3 mm intervals, using a simple linear movement in both sagittal and coronal planes. Cavernous sinography was performed via a frontal vein and using submento-vertical and subtraction views (Macpherson, 1981). Axial CT scanning of the pituitary region was performed before and after enhancement with intravenous contrast (50 ml). The high definition mode was used and either a 5 or 10 mm collimator. Carotid angiography was performed in one patient in whom sinography had suggested a medially curving carotid artery. Two patients had basal cisternography in order to define the size of a suprasellar extension which had been shown by CT.

Each patient underwent trans-sphenoidal microsurgical exploration. During the operation the surgeon noted the state of the anterior wall and the floor of the pituitary fossa. In each patient a discrete adenoma of the pituitary was identified and confirmed by histology. At the end of the operation the site and size of the tumour were recorded on diagrams.

Each type of radiological examination was reviewed without reference to the results of the other studies and then compared with the surgical findings. The plain films and tomographic findings were first compared with the report of the state of the bony fossa as noted at operation, and then to the diagrams of the tumour site and size for localization assessments. The cavernous sinogram and CT reports were compared only with the diagrams. An analysis was then made to determine the value and reliability of each radiological technique in indicating the

TABLE I

RELATION OF RADIOLOGICAL RESULTS TO SURGICAL FINDINGS

	Plain film	Tomography	Cavernous sinography	Computed tomography
Normal not confirmed	5	0	3	25
Normal confirmed	17	15	18	0
Abnormal confirmed	8	12	5	4
Borderline confirmed	0	1	0	0
Borderline not confirmed	0	1	0	0
Abnormal not confirmed	0	1*	4†	1
	30	30	30	30

*Although there was no surgical confirmation, the tumour did lie in relation to the area considered to be eroded.

†Although there was no surgical confirmation of lateral tumour extension the tumour did lie adjacent to the site considered to be abnormal in three cases.

presence of a tumour and in accurately identifying its site within the gland.

RESULTS

The results are summarized in Table I.

Radiological criteria for abnormality and correlation with surgical findings

Plain film appearances. The pituitary fossa was considered to be abnormal if it showed either general enlargement, localized bulging, localized thinning and/or erosion of the lamina dura. The so-called "double floor" appearance on the lateral view was not regarded as an abnormality because many normal fossae show multiple lines of lamina dura, depending on their contour. That such multi-flooring was due to a normal concavity or convexity was usually appreciated from the frontal views, which were also useful in showing whether the junction of the sphenoid sinus septum with the floor of the fossa had an emarginate appearance, another cause of apparent multi-flooring. The frontal view was used to confirm that a depression was pathological by demonstrating that it had produced a sharp lateral edge to the floor of the fossa.

An abnormality was seen on plain films in eight of the 30 cases; generalized enlargement ($n=8$); localized bulging ($n=6$). In each of these cases the radiologically identified abnormality was confirmed by the surgeon's observations during operation but in an additional five patients, although no abnormality was seen on plain films, a distinct abnormality was identified at operation. There was therefore an 82% agreement between radiological findings and the surgeon's observations of the fossa.

Tomography. The criteria for identifying abnormalities on the tomograms were similar to those applied to the plain films. Changes interpreted as definitely abnormal were seen in 13 patients; these included the eight patients with abnormal plain films. Local erosions were seen in four; local bulges in seven and erosions plus bulges in two. The radiological abnormality correlated with the appearance of the fossa as observed at operation in 12 of these cases. In one case the region which appeared abnormal radiologically was considered by the surgeon to be within normal limits but proved, in fact, to be closely related to the position of the tumour in the gland. Two patients showed what were regarded as borderline changes; one had a slight localized bulge anteriorly on the right without thinning of the lamina dura and the presence of an abnormality was confirmed at operation. The other had bowing back of the dorsum as the sole abnormality but only a very small tumour (3 mm) was found, located in another part of the gland. In 15 patients in whom tomography appeared completely normal the surgeon's opinion was in agreement.

In summary, in 28 patients (93%) the results of the radiological examination were in agreement with the surgeon's findings. Moreover, the abnormalities which the surgeon discovered in five patients with normal plain films were clearly shown in these patients' tomograms.

Value of plain films and tomography in localizing the tumour

The localization of the tumour inferred from the plain film abnormalities was confirmed in seven of the eight cases. The abnormality seen in the anterior wall of the final patient was caused by partial intrasellar cisternal herniation.

Of 13 patients with confirmed tomographic abnormality, this was closely related to the site of the tumour in 12, the other being the intrasellar cisternal herniation referred to above. One of the borderline erosions, not confirmed at surgery, was directly related to the tumour position; however, in the other case with bowing of the dorsum, a small 3 mm central tumour was found. The overall correlation was correct in 13 out of 15 (86%).

Correlation between abnormalities and tumour size

There was a clear tendency for radiological abnormalities to be associated with larger tumours. This is illustrated in Fig. 1. In 16 patients whose prolactinoma was estimated to be less than 5 mm in diameter, an abnormality was seen in only two (12%). By contrast, radiological abnormalities were present in 11 of the 14 patients with larger tumours (78%). The smallest tumour which produced an abnormality on tomography was 3 mm in diameter, and the largest with normal appearances measured 8 mm. That there is such overlap presumably reflects the importance of the position of the tumour in relation to the wall of the pituitary fossa in determining whether bone changes are produced.

Cavernous sinography

The cavernous sinogram was considered to be abnormal if there was a local indentation into the medial wall of the sinus. Such an impingement was considered to be present in nine cases. In five of these a laterally projecting tumour was identified during the operation; in three the tumour lay adjacent to the region thought to be abnormal but in one the tumour was in another part of the gland.

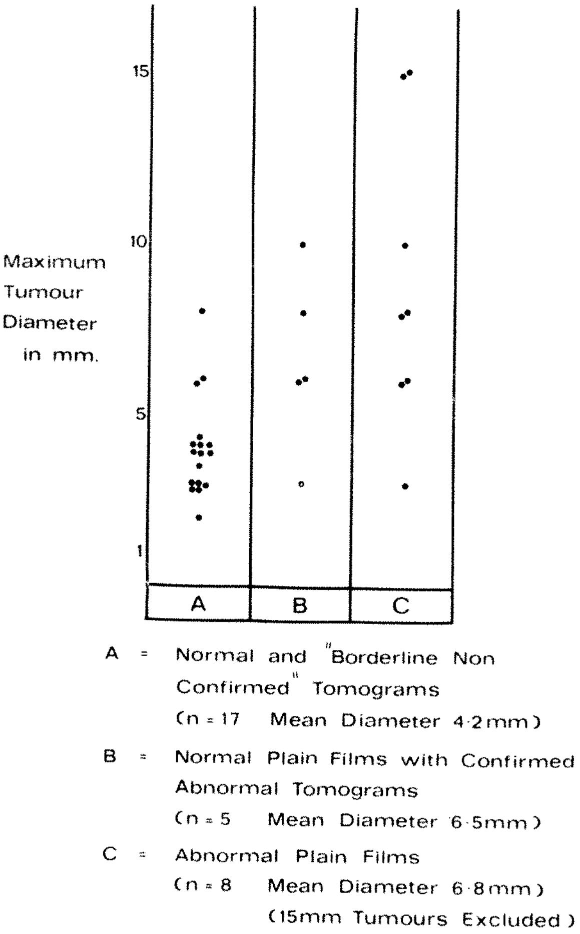


FIG. 1.

The relationship between tumour size and plain film and tomographic abnormalities.

In 21 cases, cavernous sinography was considered to be normal. In 14 of these the surgeon found the tumour to lie centrally in the gland; in four the tumour lay laterally but was not bulging laterally, while in the remaining three a small impingement into the cavernous sinus was noted at operation. Sinography demonstrated an impingement into the cavernous sinus in only one patient whose plain films and tomograms were normal. The overall agreement based on the surgical findings, as to whether or not sinography would have been expected to show abnormality was 76%.

In an additional six cases, although there was no obvious impingement into the cavernous sinus, there was bowing of either the inferior or posterior intercavernous sinus, but in only one instance was this appearance related to an adjacent tumour.

Computed tomography

The CT appearance was considered to be abnormal if there was enlargement of the fossa and/or altered density in the sellar or perisellar region on either the plain or post-contrast scan. An abnormality was seen in five cases. One patient showed an area of calcification within the pituitary fossa, another had a soft tissue mass projecting into the sphenoid sinus and in two the fossa was slightly enlarged with evidence of a soft tissue mass, both in the fossa and in the suprasellar cistern. Neither of these patients had visual impairment. The validity of these appearances was confirmed at operation in each of these four patients. In a further patient who appeared on CT to have a tumour in the left of the pituitary gland, the lesion was found at operation to be on the right. CT abnormalities were identified in only five cases (16%) and were misleading in one of these.

DISCUSSION

The results of this detailed analysis confirm that a patient with hyperprolactinaemia may have a prolactinoma without any identifiable radiological abnormality. On the other hand, endocrine criteria are not an infallible method of detecting these tumours (Teasdale *et al.*, 1980), and the value of these tests is a matter of dispute (Anon., 1980a; Anon., 1980b). Radiological methods are therefore likely to continue to be important in the investigation of this disorder, irrespective of whether it is treated by medical or surgical methods. Because the patients in the present series were selected for exploration on endocrine grounds, it is possible to determine how closely minimal radiological abnormalities were reflected in operative findings, both in terms of confirmation of the presence of abnormalities and also in the localization of a small tumour. We shall discuss the results of each radiological technique in turn and then suggest a protocol for radiological assessment of patients with hyperprolactinaemia.

Plain films

It is clear from our results that a microadenoma may produce endocrine disorders before it is large enough to cause generalized enlargement of the fossa and there is agreement that measurements of sellar area and volume are not reliable indicators of the presence of a pituitary microadenoma (Newton and Richmond, 1980). We found an abnormality on plain films in 27% of patients, but in a further 17% plain films failed to identify pituitary fossa abnormalities which were discovered by tomography and confirmed at surgery. On the other hand, in each patient in whom we identified an abnormality of the fossa on plain films, the appearances were confirmed at surgery. Plain film changes can thus be a useful indication, both of the presence of a tumour, and that it is of sufficient size to show abnormalities in other investigations. In previous reports the incidence of abnormality on plain films in patients with prolactinomas has ranged from 30–50% (Vezina and Sutton, 1974; Robertson and Newton, 1978).

Tomography

With linear tomography we found an abnormality that could be confirmed at surgery in 43% of the present series. In one further patient a radiological abnormality was present which was related to the site of the tumour even though the surgeon considered the fossa to be normal. The 43% incidence of abnormal tomography is much lower than that of 95–100% reported in previous studies (Richmond *et al.*, 1980; Robertson and Newton, 1978; Vezina and Sutton, 1974). This relatively low incidence of abnormalities is almost certainly accounted for by patients in this series having been selected for exploration on endocrinological grounds and so containing more patients with small tumours than in previous reports. In our series the mean diameter of the tumour in patients whose tomograms were abnormal was 6.7 mm, as compared to 4.2 mm in those whose fossa was normal. In a series reported by Newton and Richmond (1980), 47% of the tumours were greater than 10 mm in diameter, while Bernasconi *et al.* (1980) explored the fossa only in patients with tomographic abnormality and the smallest tumour they found was 5 mm in diameter.

Multi-directional tomography has been recommended by many authors but was not available to us. However, Swanson and du Boulay (1975) reported that changes supposedly characteristic of a pituitary tumour could be found on the tomograms of 16% of normal subjects. They suggested that hypocycloidal tomography was even more likely than linear tomography to show insignificant, borderline variants. The significance of these changes is in debate. Swanson and du Boulay concluded that their incidence was too high to be due to unrecognized pituitary tumours. However, microadenomas are present in a surprisingly high proportion of pituitary glands when studied in routine post-mortem series (Costello, 1936), although there is a poor correlation between the presence of these lesions and local radiological abnormalities (Burrow *et al.*, 1981).

The high correlation found in our series between the location of radiological changes, either on plain films or tomography, and the position of the tumour confirms previous reports (Bernasconi *et al.*, 1980; Newton and Richmond, 1980). The reliability of these changes clearly make them a useful guide to the area that should be the focus of exploration at operation.

Cavernous sinography

When the cavernous sinogram was abnormal the tumour was on the same side as the impingement in a high proportion of cases (90%). In most of these patients there was a lateral extension of the adenoma. However, the sinogram was normal in other patients who had either small lateral extensions or laterally placed tumours. A positive result, therefore, can localize the lesion, but a negative one does not exclude lateral extension.

Théron *et al.* (1979) reported that bowing of either the inferior or posterior intercavernous sinuses was a useful indication of the presence of a pituitary adenoma. Their report does not state whether this observation was confirmed at surgery. In our series we were unable to relate these appearances to the presence of an adjacent tumour.

As tomography was abnormal in all but one of the cases with cavernous sinus abnormality, sinography does not contribute appreciably to the detection of a microadenoma. However, it does identify positional

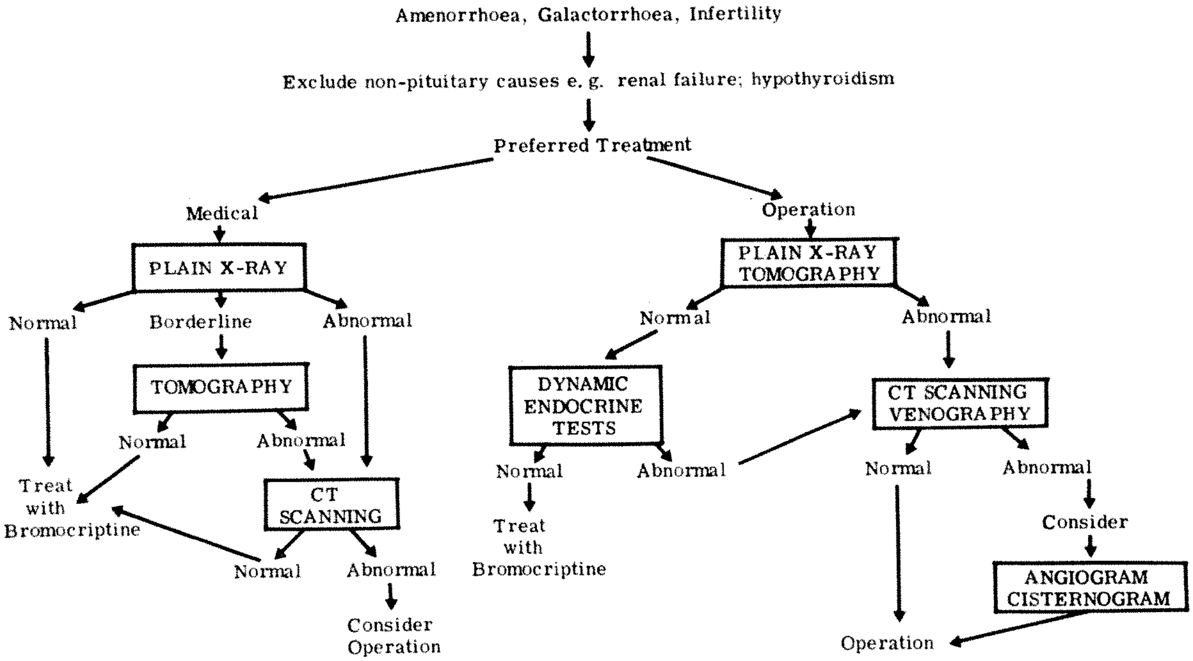


FIG. 2.

Suggested protocol of radiological investigation of prolactin secreting microadenomas based on preferred treatment.

abnormalities or aneurysmal dilatation of the carotid arteries and can therefore be used as an alternative to carotid angiography in the assessment of patients selected for operative treatment.

Computed tomography

Demonstration of a pituitary microadenoma by CT depends on the equipment and format used, as well as on the size and density of the lesion. In our series the only completely intrasellar tumour detected by CT was identified because it was calcified. CT gave information additional to that provided by tomography only in the two cases that showed suprasellar extension, both of whom had abnormal plain films. Others (Belloni and Maira, 1980; Leonardi *et al.*, 1980; Syvartsan *et al.*, 1979) have claimed to be able to diagnose intrasellar pituitary microadenomas by CT but few have obtained accurate corroboration of their findings; in many cases it is difficult to distinguish the normally enhancing infundibulum from the supposed tumour. Our experience accords with that of Richmond *et al.* (1980) who stated that with their equipment they could not demonstrate either intra- or parasellar structures in sufficient detail to show a small tumour.

Although CT scanning may not diagnose the microadenoma it may still be useful in selected patients in order to exclude a hypothalamic lesion and to identify possible cases of intrasellar cisternal herniation (ISCH). It should also be performed when a patient with an obviously abnormal fossa is treated medically, because it will sometimes show a suprasellar lesion even in the absence of changes in the visual fields. Such patients may be those at greatest risk of visual failure should pregnancy be achieved.

Pneumo-encephalography/basal cisternography

Basal cisternography/ventriculography (Macpherson, 1980) was performed in two of our patients in order to assess the suprasellar extension demonstrated by CT. In a total experience now of over 40 patients with prolactinomas only once has intrasellar cisternal herniation (ISCH) been obvious at operation and it did not prevent removal of the tumour. Although others (Richmond *et al.*, 1980) have reported that ISCH can be detected by air studies or cisternogram in 24% of patients with prolactinoma, we have not included this investigation as routine. In this series the finding of such an abnormality would not have influenced the decision whether or not to operate because this was taken on endocrinological grounds.

CONCLUSIONS AND RECOMMENDATIONS

If careful assessment of plain films or tomograms from a patient suspected of having a prolactinoma shows either localized erosion or bulge in the pituitary fossa, these are reliable signs of the presence of a tumour, and usually also of its site. Cavernous sinography on the other hand is of no additional value in the detection of small tumours but may be useful in order to assess the state of the carotid arteries pre-operatively. Likewise, CT is useful only in larger tumours where it may show suprasellar extension and need only be performed for this purpose when plain films are abnormal. However, it is probably prudent to advise pre-operative CT to exclude other pathology. The extent of radiological investigation which is appropriate depends upon whether the patient is to have medical or surgical treatment, and we propose a protocol, as illustrated in Fig. 2.

REFERENCES

ANONYMOUS, 1980a. Trends in the management of prolactinomas. *British Medical Journal*, *281*, 338–339.

1980b. Hyperprolactinaemia: pituitary tumour or not? *Lancet*, *i*, 517–519.

BELLONI, G., and MAIRA, G., 1980. Minor structural changes in intrasellar pathology: a radiological diagnostic problem. In *Pituitary Microadenomas*, Ed. G. Faglia, M. A. Grovanelli, and R. M. MacLeod (Academic Press, New York), pp. 337–346.

BERNASCONI, V., BETTINELLI, A., and VACCARI, U., 1980. Prolactin-secreting pituitary microadenomas: tomographic assessment of normal sella on plain skull films. In *Pituitary Microadenomas*, Ed. G. Faglia, M. A. Grovanelli, and R. M. MacLeod (Academic Press, New York), pp. 323–328.

BURROW, G. N., WORTZMAN, G., REWCASTLE, N. B., HOLGATE, R. C., and KOVACS, K., 1981. Microadenomas of the pituitary and abnormal sella tomograms in an unselected autopsy series. *New England Journal of Medicine* (In press).

COSTELLO, R. T., 1936. Subclinical adenoma of the pituitary gland. *American Journal of Pathology*, *12*, 205–215.

COWDEN, E. A., THOMSON, J. A., DOYLE, D., RATCLIFFE, J. G., MACPHERSON, P., and TEASDALE, G. M., 1979. Tests of prolactin secretion in diagnosis of prolactinomas. *Lancet*, *i*, 1155–1158.

LEONARDI, M., BERTOLISSI, F., PENCO, T., FABRIS, G., and DE NARDI, F., 1980. CT evidence of functioning microadenomas in the pituitary. In *Pituitary Microadenomas*, Ed. G. Faglia, M. A. Grovanelli, and R. M. MacLeod (Academic Press, New York), pp. 329–335.

MACPHERSON, P., 1980. Combined metrizamide ventriculogram and basal cisternogram via suboccipital route. *British Journal of Radiology*, *53*, 733–734.

1981. Improvements in techniques developed over a series of 500 orbital venograms–cavernous sinograms. *Clinical Radiology*, *32*, 107–111.

NEWTON, T. H., and RICHMOND, I., 1980. Correlation between radiographic and surgical findings in prolactin secreting adenomas. In *Pituitary Microadenomas*, Ed. G. Faglia, M. A. Grovanelli, and R. M. MacLeod (Academic Press, New York), pp. 313–322.

RICHMOND, I., NEWTON, T. H., and WILSON, C. B., 1980. Prolactin secreting pituitary adenomas: correlation of radiographic and surgical findings. *American Journal of Roentgenology*, *134*, 707–710.

ROBERTSON, W. D., and NEWTON, T. H., 1978. Radiological assessment of pituitary microadenomas. *American Journal of Roentgenology*, *131*, 489–492.

SWANSON, H. A., and DU BOULAY, G., 1975. Borderline variants in the normal pituitary fossa. *British Journal of Radiology*, *48*, 366–369.

TEASDALE, G. M., RATCLIFFE, J. G., THOMSON, J. A., and COWDEN, E. A., 1980. The prolactinoma problem. *Lancet*, *i*, 925–926.

THÉRON, J., CHEVALIER, D., DELVART, M., and LAFFONT, J., 1979. Diagnosis of small and micro-pituitary adenomas by intracavernous sinus venography. *Neuroradiology*, *18*, 23–30.

VEZINA, J. L., and SUTTON, T. J., 1974. Prolactin-secreting pituitary microadenomas. *American Journal of Roentgenology*, *120*, 46–54.

1981, *British Journal of Radiology*, 54, 572–575

Vascular anatomy in the suboccipital region and lateral cervical puncture

By T. C. S. Cox, F.R.C.R.

Middlesex Hospital, London WC1

J. M. Stevens, F.R.C.R., M.R.C.R. and B. E. Kendall, F.R.C.P., F.R.C.R.

National Hospital for Nervous Diseases, London WC1

(*Received January 1981*)

ABSTRACT

The theoretical risk of injuring the vertebral artery or anomalous vessels at lateral cervical puncture is assessed. In just less than 30% of vertebral arteries the vessel overlies the lateral aspect of the spinal canal between the first and second cervical vertebrae, usually the antero-inferior quadrant. Directing the spinal needle to the posterior third of the canal virtually eliminates the possibility of injuring this and most anomalous arteries traversing the region. The likelihood of inducing subarachnoid haemorrhage by injuring these vessels would appear to be considerably less in lateral cervical than in cisternal puncture.

The acceptance of a water-soluble contrast medium for cervical myelography has led to the widespread use of lateral cervical puncture between the first and second vertebrae (C1–2) in appropriate cases. Images of the cervical cord, nerve roots and subarachnoid vessels are generally better when water-soluble contrast medium is introduced by this route than when it is transported from the lumbar region. The puncture is performed by advancing a 22 gauge lumbar puncture needle horizontally from the lateral side of the neck towards the posterior third of the spinal canal, using intermittent fluoroscopy where necessary to check the position, until the dura is punctured and cerebrospinal fluid obtained.

Personal experience and that of other workers (Amundsen and Skalpe, 1975; Skalpe and Amundsen, 1975; Sackett *et al.*, 1977; Sackett, 1978) has shown the lateral cervical puncture to be a simple and, in practice, safe approach to the subarachnoid space. Notwithstanding, there is a theoretical risk of injuring the spinal cord and any significant blood vessels traversing the region. On vertebral angiograms anomalous arteries are occasionally shown within the theca at the C1–2 level and here the vertebral artery itself may overlie the lateral aspect of the spinal canal. With the increasing popularity of lateral cervical puncture among general radiologists as well as neuroradiologists, we considered it pertinent to assess the incidence of such vessels and hence the theoretical risk of puncturing a vertebral artery or one of its major branches either lateral to or within the spinal theca. Documentation is provided, as far as we are aware for the first time, of the variation in position of the vertebral artery as it overlies the C1–2 space.

MATERIAL AND METHOD

Vertebral angiograms performed at the Middlesex Hospital and National Hospital for Nervous Diseases were surveyed. Patients with tonsillar depression from any cause were excluded, but otherwise the cases were selected only so far as they showed the upper cervical region with no more than a minimum of head rotation and tilt. A total of 558 vertebral arteries from 396 patients were examined. All vertebral arteries were grouped according to their position with respect to the spinal canal at C1–2 in the lateral projection; vessels in group 1 lay anterior to the canal and those in groups 2, 3 and 4 overlay the anterior, middle and posterior thirds of the canal respectively (Fig. 1). The distribution of

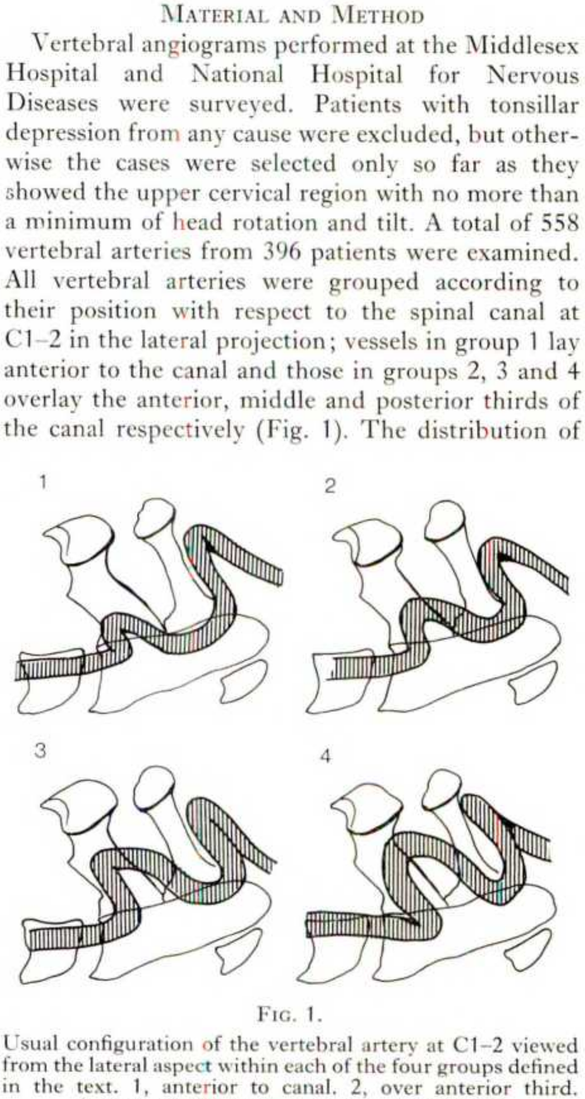


FIG. 1.

Usual configuration of the vertebral artery at C1–2 viewed from the lateral aspect within each of the four groups defined in the text. 1, anterior to canal. 2, over anterior third. 3, over middle third. 4, over posterior third.

arteries within the four groups was related to side in 489 vessels, to sex in 388 and to age in 126. Finally the relationship of the posterior inferior cerebellar artery (PICA) to the foramen magnum and atlanto-occipital membrane was assessed in 285 angiograms.

RESULTS

At C1–2, 72.2% of vertebral arteries lay anterior to the spinal canal. Of the remainder, 19.0% overlay the anterior third, 7.3% the middle third and 0.9% the posterior third of the canal. Figures 2, 3 and 4 indicate graphically how this distribution was affected by considerations of side, sex and age.

The PICA arose below the foramen magnum in 8.8%. In only two cases was the origin below C1. The caudal loop extended below the foramen magnum in 14.7% but no loop descended below C1. In the 558 vertebral arteries studied, no case of fenestration was encountered.

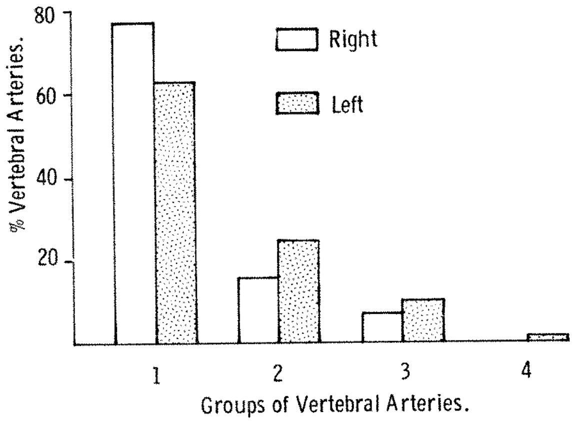


FIG. 2.

Percentage distribution of left and right vertebral arteries within four groups defined according to their position with respect to the spinal canal viewed from the lateral aspect.

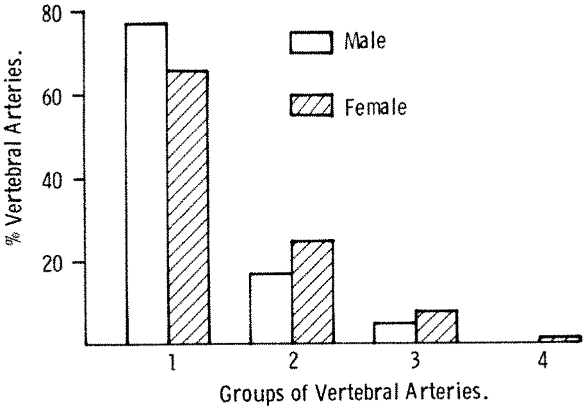


FIG. 3.

Percentage distribution in the four groups in males and females.

Other observations regarding extraspinal muscular arteries, epidural veins and spinal arteries were made incidentally, and they are recorded in the discussion which follows.

DISCUSSION

Lateral cervical puncture was originally used to perform percutaneous cervical cordotomy (Rosomof *et al.*, 1965). Its accepted safety led to employment of the technique for introducing myelographic contrast medium (Kelly and Alexander, 1968). In the earlier descriptions the needle was advanced towards the anterior third of the spinal canal at C1–2 which allegedly reduced the risk of injuring the cord as the dura was punctured. To our knowledge no neurological complications from the actual puncture have been published.

The possibility of injuring a major vessel such as the vertebral artery has been appreciated (Kelly and Alexander, 1968). Because of the intimate association of the vertebral veins, which form a plexus around the extra-arachnoid part of the artery, arterio-venous fistula is the most frequent complication of transfixing these vessels. Bleeding from a small puncture wound in the artery lying between the foramina transversaria is most unlikely to pass along the needle track and enter the theca. However within the subarachnoid space at C1–2 large anomalous arteries may be present (Rice, 1979), namely, an exceptionally low PICA, and a vertebral artery entering the spinal canal below C1 which is

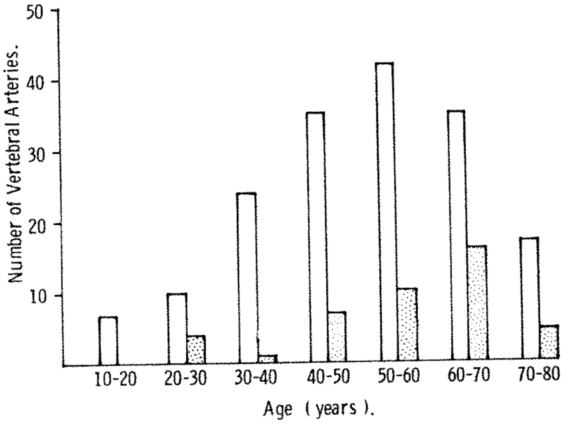


FIG. 4.

Distribution of vertebral arteries by decades. The total number of arteries examined is shown on the left and the number overlying the spinal canal in the lateral projection (shaded) on the right.

usually associated with fenestration. Serious subarachnoid haemorrhage is a rare complication of cisternal puncture and has also been described in lumbar puncture (Rice, 1979). Blood in the spinal subarachnoid space is known to cause cerebral vasospasm (Echlin, 1971) and this event is a recorded complication of myelography (Smith *et al.*, 1973).

The vertebral artery frequently presents a dorsal curve as it emerges from the transverse foramen of C2 before inclining ventrally again to enter the transverse foramen of C1. This dorsal curve is confined beneath the obliquus capitus inferior muscle, and in about 30% of arteries overlies the spinal canal and becomes a direct lateral relation to it. In the majority, however, the vessel overlies the antero-inferior quadrant of the canal and it is in this region that it is most likely to be encountered at lateral cervical puncture (Fig. 1). To avoid injuring the vessel, therefore, it is recommended that the needle be directed towards the posterior third of the spinal canal, as preferred by other authors (Amundsen and Skalpe, 1975; Sackett, 1978; Rice, 1979). Special care should be taken to keep the needle away from the anterior part of the superior border of the neural arch of C2.

In about one patient in 100, the vertebral artery will overlie the posterior third of the spinal canal. Because the artery lies lateral to the canal it moves anteriorly when there is rotation of the spine to the opposite side. Therefore, by allowing a small amount of rotation away from the side of the puncture the occasional vertebral artery still at risk should be avoided.

Large dorsal curves in the vertebral arteries at C1–2 are more likely to be encountered on the left than the right and in patients over 50 (Figs. 2 and 4), but the numbers in our study were too small for any recommendations to be based on these considerations.

Rice has indicated that anomalous intrathecal arteries at C1–2 lie anterior to the dentate ligament, and therefore will not be endangered by approaching the posterior third of the spinal canal (Rice, 1979). However an anomalous PICA may lie in the middle third of the canal and encroach upon the posterior third (Fig. 5). The PICA is far less likely to be encountered in lateral cervical than cisternal puncture. In this series we observed that caudal loops of the PICA extending below the foramen magnum lie invariably in the posterior half of the spinal canal; indeed in over 10% of vertebral arteries surveyed the PICA loop lay within 3 mm of the mid-line when 5 mm or less from the position of the atlanto-occipital membrane. That lateral cervical puncture is safer and even easier to perform than cisternal puncture has been affirmed by others (Amundsen and Skalpe, 1975; Heinz and Goldman, 1972).

Though fenestrated vertebral arteries are occasionally encountered in our routine practice (Fig. 6), none was present in this series. This reflects a considerably lower incidence than the 2.2% reported

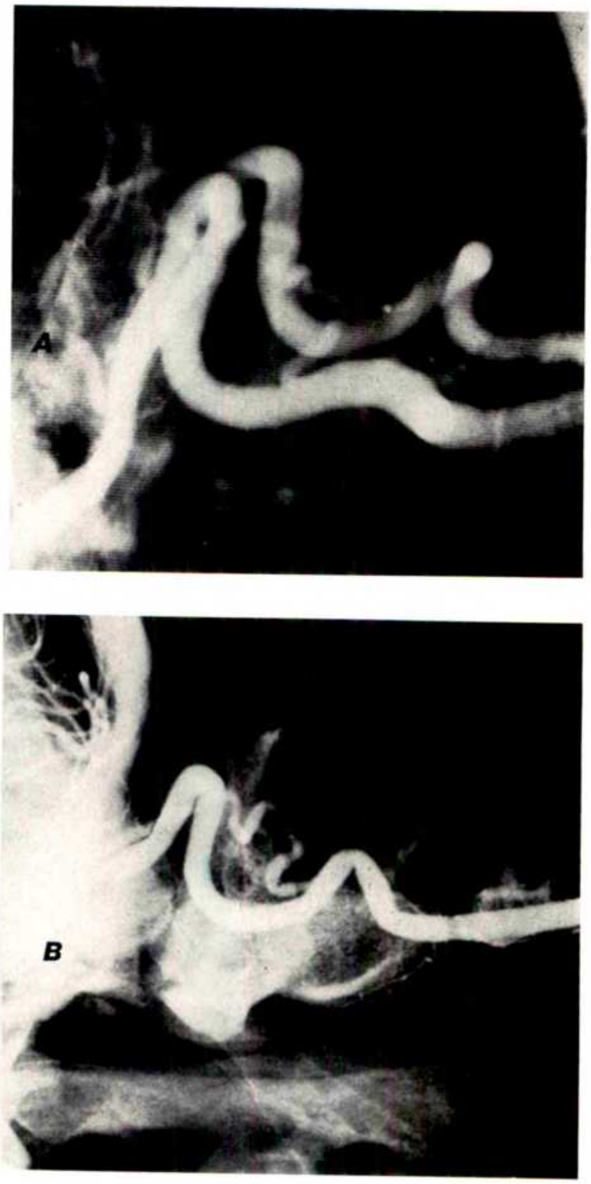


FIG. 5.

Two patients with anomalous postero-inferior cerebellar arteries within the spinal canal at C1–2. In A, the vessel just encroaches on the posterior third of the canal; slight rotation of the spine is present projecting the relevant vertebral artery anterior to the spinal canal.

in Japanese patients (Kowada *et al.*, 1972). The anomalous vessel, in our experience, and in illustrated examples (Kowada *et al.*, 1972; Rice, 1979), may be avoided by approaching the posterior third of the canal with the spinal needle.

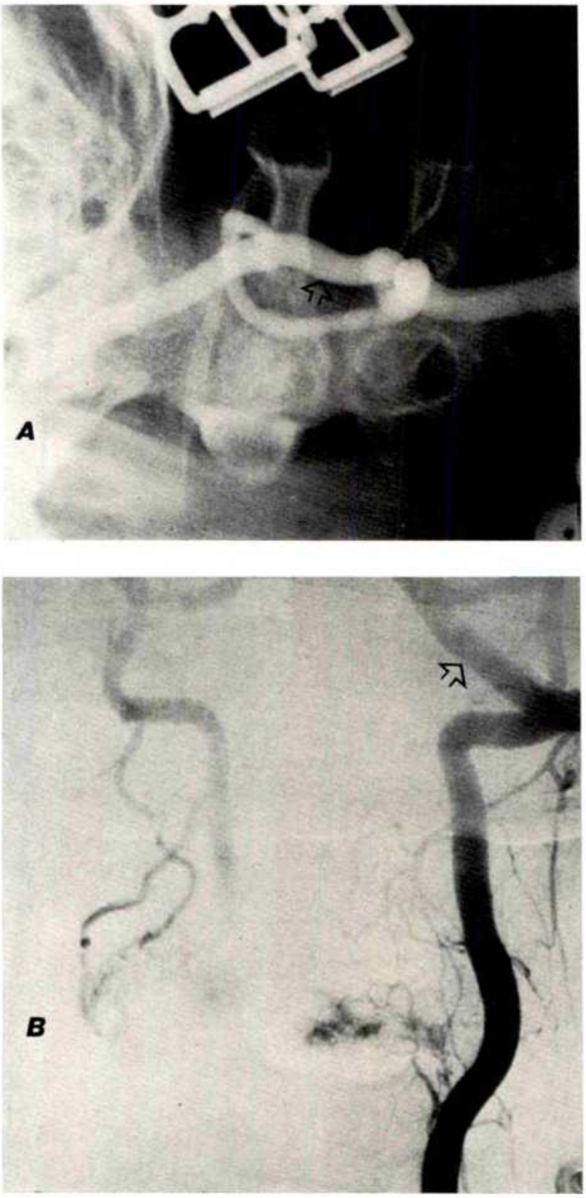


FIG. 6.

Fenestrated vertebral artery in which the larger component of the fenestration enters the spinal canal, and presumably becomes subarachnoid, between C1 and C2. (An angioma is visible in the antero-posterior subtraction view, the investigation of which was the indication for angiography in this particular case.)

Other vascular structures may be seen over the C1–2 space. Extraspinally there are muscular branches of the vertebral, but curiously enough, these vessels usually leave an avascular "window" between C1 and C2. Large epidural veins are occasionally seen dorsal to the theca but they do not pose a significant problem if punctured. Careful technique designed to avoid trauma to the cord will also avoid trauma to the anterior and posterior spinal arterial chains lying on its surface.

CONCLUSION

Our study has confirmed that the theoretical risk of producing significant vascular injury at lateral cervical puncture is very low, provided the posterior third of the spinal canal is approached. The anterior part of the canal near the superior border of the arch of C2 should particularly be avoided and slight rotation of the patient away from the side of the puncture is suggested to minimize further the possibility of injuring the vertebral artery.

REFERENCES

AMUNDSEN, P. and SKALPE, I. O., 1975. Cervical myelography with water soluble contrast medium (metrizamide). *Neuroradiology*, *8*, 209–212.

ECHLIN, F., 1971. Experimental vasospasm, acute and chronic, due to blood in the subarachnoid space. *Journal of Neurosurgery*, *35*, 646–656.

HEINZ, E. R. and GOLDMAN, R. L., 1972. The role of gas myelography in neuroradiological diagnosis. Comments on a new and simple technique. *Radiology*, *102*, 629–634.

KELLY, D. L. and ALEXANDER, E., 1968. Lateral cervical puncture for myelography. Technical note. *Journal of Neurosurgery*, *29*, 106–110.

KOWADA, M., YAMAGUCHI, K. and TAKAHASHI, H., 1972. Fenestration of the vertebral artery with a review of 23 cases in Japan. *Radiology*, *103*, 343–346.

RICE, J. F., 1979. Lateral cervical puncture for myelography: posterior approach. *Radiology*, *132*, 760–762.

ROSOMOF, H. L., CARROLL, F., BROWN, J. and SHEPTAK, P., 1965. Percutaneous radiofrequency cervical cordotomy: technique. *Journal of Neurosurgery*, *23*, 639–644.

SACKETT, J. F., 1978. Cervical and lumbar routes for metrizamide cervical examination. *Neuroradiology*, *16*, 273–274.

SACKETT, J. F., STROTHER, C. M., QUAGLIERI, C. E., JAVID, M. J., LEVIN, A. B. and DUFF, T. A., 1977. Metrizamide—CASF contrast medium. Analysis of clinical application in 215 patients. *Radiology*, *123*, 779–782.

SKALPE, I. O. and AMUNDSEN, P., 1975. Thoracic and cervical myelography with metrizamide. *Radiology*, *116*, 101–106.

SMITH, R. A., COLLIER, H. F. and UNDERWOOD, F. O., 1973. Cerebral vasospasm following myelography. *Surgical Neurology*, *1*, 87–90.

1981, *British Journal of Radiology*, 54, 576–585

Clinical applications of radionuclide lung scanning in infants and children

By *I. Gordon, M.B., B.Ch., F.R.C.R., D.M.R.D., †P. Helms, M.B., B.S., M.R.C.P. and ‡F. Fazio, Dipl. Med. e Chir.

*Department of Radiology and †Respiratory Unit, Hospital for Sick Children, Great Ormond Street, London WC1 and Medical Research Council, ‡Cyclotron Unit, Hammersmith Hospital, London W12

(*Received August 1980 and in revised form January 1981*)

ABSTRACT

Krypton 81m ventilation and technetium 99m perfusion lung scans in anterior, posterior and oblique views in 86 children (age range 14 days to 15 years) with various paediatric problems were obtained.

On reviewing these studies we found four main areas of clinical usefulness. (a) Establishing the diagnosis; in a relatively small number of patients the lung scan was essential for either establishing the exact diagnosis or directing attention to the abnormal area. (b) Refuting a diagnosis: the two main groups in this category include possible bronchiectasis and inhaled foreign body. (c) Establishing the extent of the disease; radionuclide studies enable one to assess and follow up the extent of the disease in children with lower respiratory problems; a lung scan may obviate the need for bronchography in bronchiectatics failing to respond to medical treatment and for whom surgery is being considered. Repeat studies are useful in following the natural history or the response to treatment of various lung conditions. (d) Assessing the success of surgical procedures on the heart and on abnormal pulmonary arteries.

We indicate that ^{81}Kr^{m} ventilation/^{99}Tc^{m} perfusion scanning are particularly useful in small children in whom tests of overall pulmonary function cannot be carried out because of lack of co-operation.

Reliable lung function tests are at times difficult to obtain in children. This is particularly so when significant symptoms such as coughing or dyspnoea are present. From two to six years the functional assessment of the lungs is limited by poor subject co-operation, although ingenuity and patience can yield information about the conducting airways by using a modified plethysmographic technique (Dab and Alexander, 1976) or forced oscillation methods (Cogswell, 1973; Mansell *et al.*, 1972). Recent attention has been focused on the use of forced random noise to assess the mechanical properties of lungs in young children (Williams *et al.*, 1979). All these techniques assess the overall function of the lungs and although uneven distribution of ventilation and perfusion can be demonstrated by combining tests of ventilatory function, such as nitrogen washout, and the frequency dependence of compliance or resistance with arterial oxygen tensions, the regional distribution and extent of these disturbances cannot be assessed. Using radionuclide techniques the distribution of perfusion and ventilation can be obtained in children of any age without subject co-operation.

Since the first developments in external counting of perfused and ventilated radioisotopes into the lung (Knipping *et al.*, 1955) many different agents have been used. Regional perfusion is now routinely assessed using an intravenous injection of technetium 99m macroaggregates (^{99}Tc^{m}MAA) and external recording with a gamma camera. This is a well-established technique which provides multiple high-quality images in different projections.

Ventilation studies had always been difficult to obtain in children prior to the introduction of ^{81}Kr^{m} (Fazio and Jones, 1975). Single breath washout of ^{133}Xe requires considerable patient co-operation and is therefore impractical in young children; other limitations are the relatively high radiation dose from xenon and the solubility of the isotope in the chest wall, limiting its use to single views. ^{13}N^{m} has been used in infants and children (Godfrey and McKenzie, 1977), but this radionuclide is limited in its use as it requires the immediate proximity of a cyclotron unit. ^{81}Kr^{m}, an insoluble gas, with a single energy γ emission (190 keV) and 13 s half-life, provides multiple view ventilation images directly comparable to the multiple 140 keV ^{99}Tc^{m}MAA images. Its very low radiation dose makes it an ideal radionuclide for use in children.

The clinical applications of ^{81}Kr^{m} radionuclide scanning in children have recently been described (Treves *et al.*, 1974). Using ^{99}Tc^{m}MAA and ^{81}Kr^{m}, high-quality images in multiple projections can be obtained in children of any age. The aim of this paper is to assess the clinical usefulness of the combined ^{81}Kr^{m}/^{99}Tc^{m}MAA technique in a series of 100 scans in 86 infants and children with a variety of cardiopulmonary disorders seen at the Hospital for Sick Children in 1978–79.

METHODS

Technique

In all patients, lung ventilation/perfusion scans were obtained in four views (anterior, posterior and both posterior oblique projections) with the combined ^{81}Kr^{m}/^{99}Tc^{m}MAA technique. The two anterior oblique views were performed when better visualization of the middle lobe and lingula was required or when the other four views were normal. This is described in detail elsewhere (Fazio and Jones, 1975; Fazio *et al.*, 1978) and will be only summarized here. $^{81}\text{Kr}^{m}$ is eluted with humidified air from its parent ^{81}Rb. The parent's half-life is 4.6 hours and it is cyclotron produced (Clark *et al.*, 1976). By continuously adding $^{81}\text{Kr}^{m}$ to the inspired air during normal breathing, equilibrium of the isotope with alveolar gas is never reached because of the short half-life; thus the distribution becomes representative of ventilation rather than volume. A possible exception to this may be the neonate and small infant with a high minute volume. Oblique views were chosen in preference to the lateral views customary in adult subjects because of the increased problems relating to "shine through" activity from

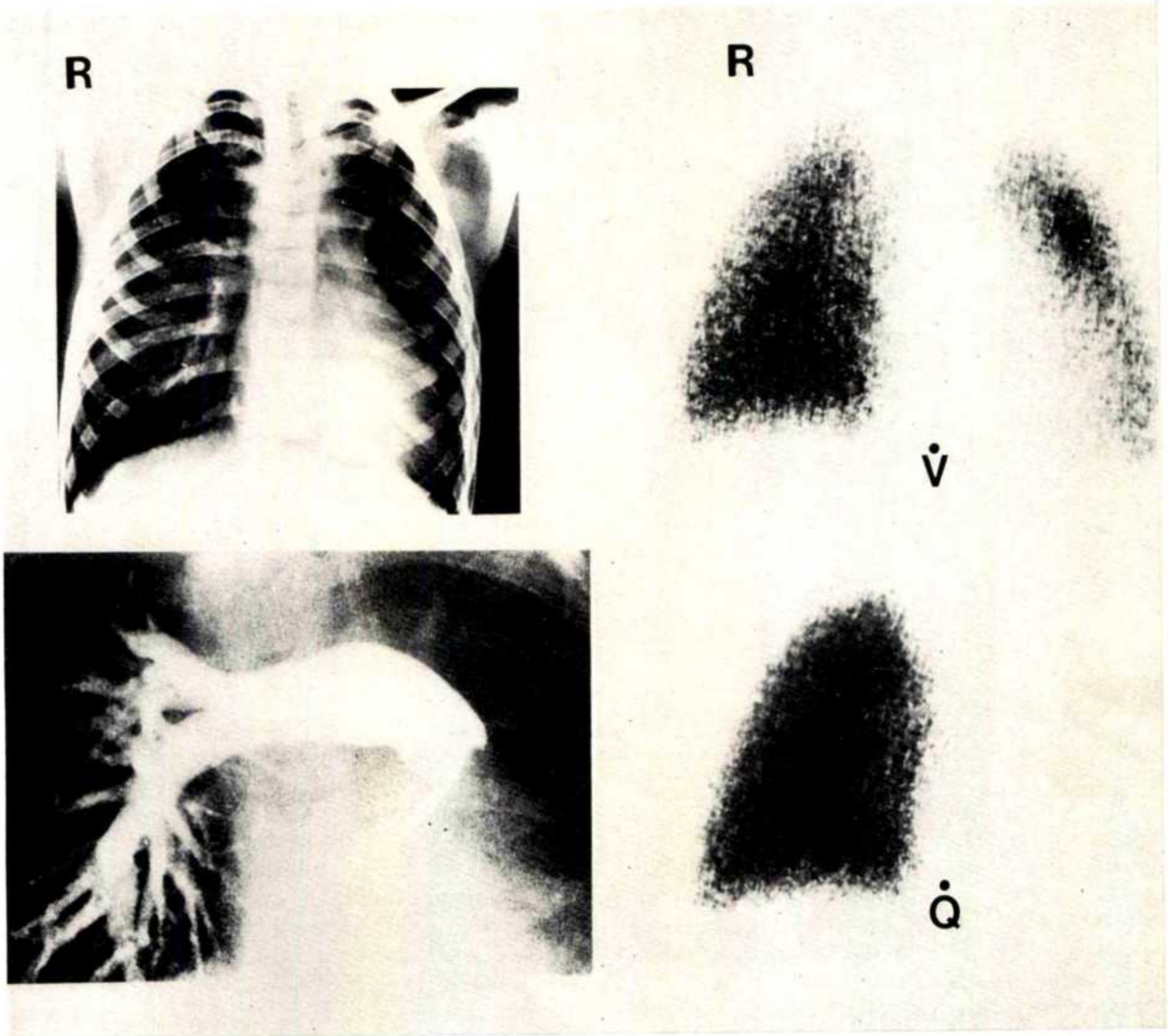


FIG. 1.

Chest radiograph, pulmonary angiogram and ventilation ($\dot{V}$)/perfusion ($\dot{Q}$) scan in a nine-year-old child with an unsuspected absent left pulmonary artery. The radiograph shows the mediastinum shifted to the left, with a small left lung, minimal rib crowding is noted. The lung scan shows a non-perfused left lung which is moderately well ventilated. The pulmonary angiogram confirms the congenitally absent left pulmonary artery. He was thought to have damaged his left lung secondary to bronchiolitis in early infancy and was reputed to have a decreased exercise tolerance subsequently disproved by normal cardio-respiratory responses to formal exercise testing on a bicycle ergometer. The only abnormality found on respiratory function testing was an increased dead space/tidal volume ratio.

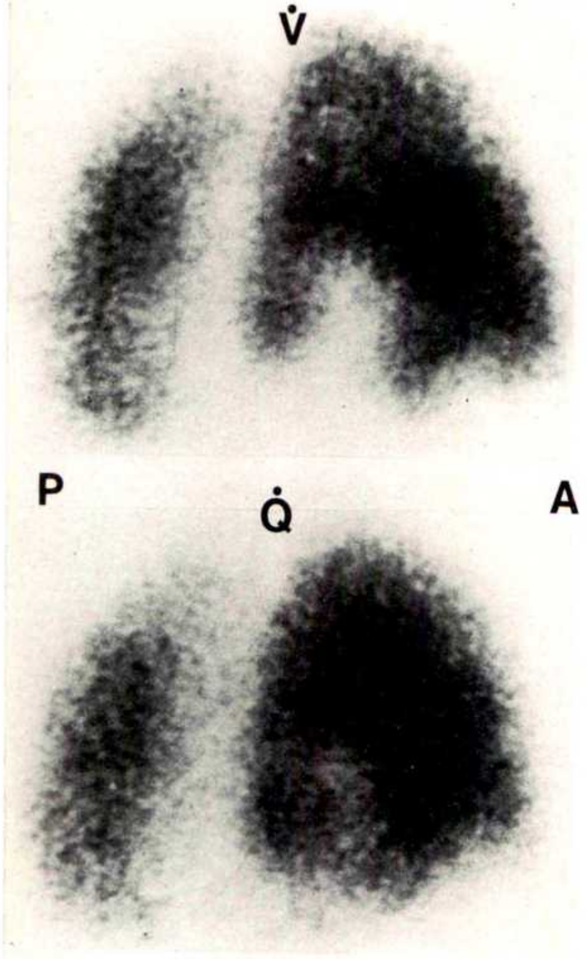


Fig. 2.

Right posterior oblique ventilation ($\dot{V}$) and perfusion ($\dot{Q}$) lung scans in a 14-year-old girl with haemoptysis and right sided chest pain following a termination of pregnancy. The scan shows well matched defects on both images, best seen in the right lower lobe. She also had phenylketonuria and perennial asthma. Pulmonary function studies showed gas trapping and airflow obstruction.

the contra-lateral lung when scanning small children.

The procedure for obtaining the combined ventilation/perfusion scans involves a single intravenous injection of ^{99}Tc^{m}MAA with the infant/child lying supine over the gamma camera. Macroaggregates were used during the period described in this paper although we now use microspheres. The median particle size was 50 μ and quality control was carried out at weekly intervals. The methods used included paper chromotography and microscopy.

A soft rubber face mask which is connected to the outflow of the ^{81}Kr^{m} generator is applied for each ^{81}Kr^{m} ventilation scan. (The radiation dose of ^{99}Tc^{m}MAA is based on an adult dose of 37 MBq (1 mCi) and scaled down according to body surface area.) All infants under 12 kg in body weight receive a minimum of 13 MBq (0.35 mCi) of ^{99}Tc^{m}MAA; 200 000 counts are collected with the window of the gamma camera set for the 140 keV of ^{99}Tc^{m} and a perfusion image is recorded on radiographic film. Without moving the patient, a flow of ^{81}Kr^{m} is added to the face mask and the window switched to 190 keV. A ventilation image is then obtained by collecting another 200 000 counts. Spillover of ^{99}Tc^{m} into the ^{81}Kr^{m} window is less than 3%. The patient is repositioned and the same sequence is repeated for other views. Throughout the procedure a portable electric fan blows the expired ^{81}Kr^{m} away from the camera face. The total time required for a full ventilation/perfusion study in four views is 20 minutes. Immediately following the lung scan, standard frontal and lateral chest X-rays are obtained.

The whole-body absorbed radiation dose derived from the ^{81}Kr^{m} ventilation study (four views) is less than 0.006 mGy (0.6 mrad) for an adult and 0.013 mGy (13 mrad) for an infant; the dose to the target organ (lungs) is 0.16 mGy (160 mrad) for a 14-year-old and 0.72 mGy (720 mrad) for a one-year-old (Myers, personal communication). Whole-body absorbed dose resulting from 13 MBq (1 mCi) injection of ^{99}Tc^{m}MAA in an adult is less than 0.04 mGy (40 mrad) with a target organ dose of less than 0.28 mGy (280 mrad) (Chandra *et al.*, 1973). There is no finally accepted dose of ^{99}Tc^{m}MAA for use in children and it is an attempt to obtain satisfactory images with the least possible amount of radionuclide that has led us to use an adult dose of 37 MBq (1 mCi) and scale this down according to the body surface area.

Patients

One hundred scans were carried out in 86 patients who were referred for evaluation by the respiratory physicians and cardiologists (Table I). The age groups of the children studied are shown in Table II. Very young children below one-and-a-half years were sedated with chloral hydrate (50 mg/kg). The usefulness of the scan was judged by its ability to: (a) establish or refute a diagnosis; (b) assess the extent and regional distribution of lung disease; (c) assess the treatment.

Assessment of scans

This involved two of the authors (I.G. and P.H.) in viewing the images and describing the distribution of ventilation and perfusion on a lobar and subsegmental basis. The anatomical information provided

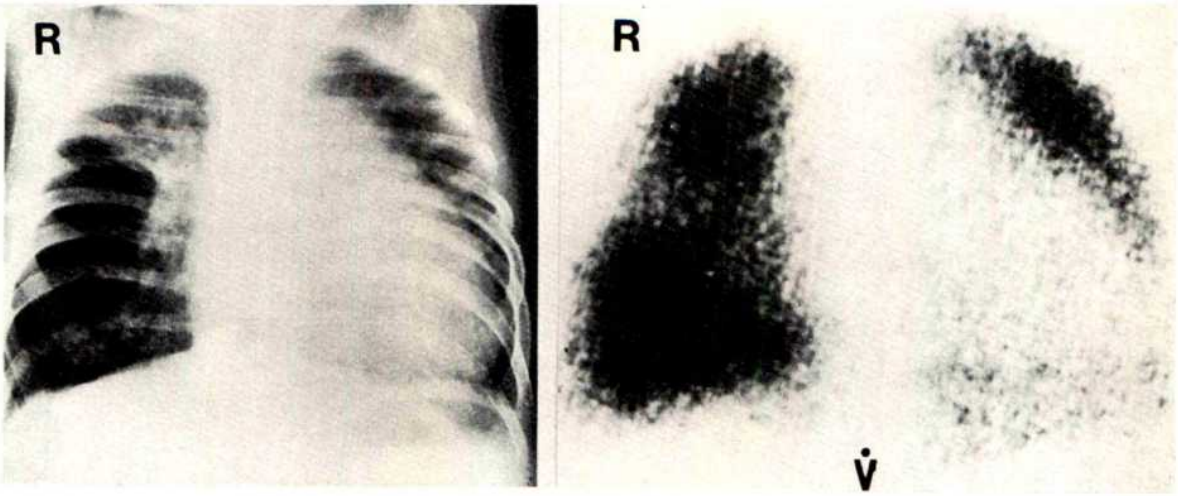


FIG. 3.

AP chest radiograph and an anterior ventilation ($\dot{V}$) lung-scan in a four-month-old infant with a single ventricular septal defect and in respiratory failure. The radiograph shows a large heart with pulmonary plethora. The changes in the right upper zone were thought to be chronic consolidation. The lung scan reveals absent ventilation/perfusion in the right mid-zone, *i.e.* the hypertranslucent area on the radiograph. An emphysematous right middle lobe was resected following closure of the VSD.

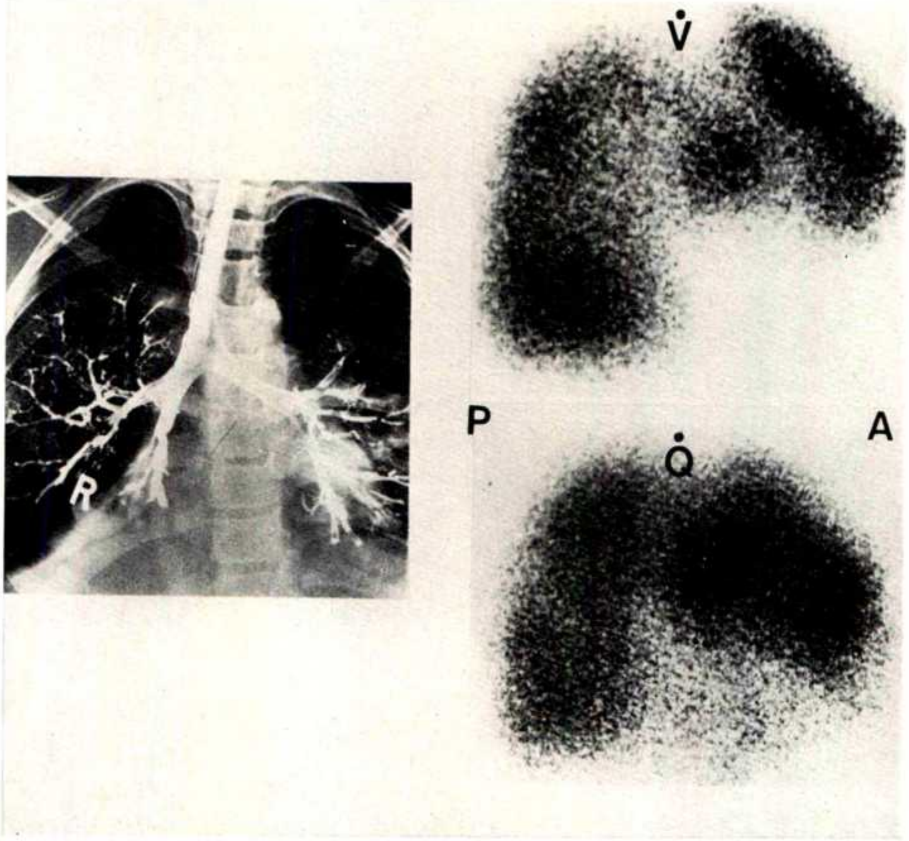


FIG. 4.

Anterior view of bilateral bronchography with right posterior oblique ventilation ($\dot{V}$) and perfusion ($\dot{Q}$) lung scans in a 13-year-old girl with severe bronchiectasis. The extensive damage in the right lower lobe is shown on bronchography and is also shown as a complete absence of ventilation, with a similar but less marked disturbance of perfusion.

TABLE I

RADIONUCLIDE LUNG SCANS: HOSPITAL FOR SICK CHILDREN 1978–79

	Patient No.	Scan No.
Cystic fibrosis	18	25
Bronchiectasis	8	8
Asthma/bronchial lability	7	9
Vascular ring	4	4
Atelectasis	6	6
Pneumonia	5	5
Lobar emphysema	5	5
Malignancy	4	6
Inhaled foreign body	4	4
Alveolitis	3	3
Obliterative bronchiolitis	3	3
Lung cysts	3	3
Hypoplastic lung	3	3
Pulmonary emboli	3	3
Hyperlucent lung	3	4
Diaphragmatic hernia	2	3
Pulmonary fibrosis	1	1
Ventricular septal defect	1	1
Familial dysautonomia	1	1
Wilson Mikity syndrome	1	1
Meconium aspiration	1	1
Total	86	100

TABLE II

AGE RANGES OF CHILDREN STUDIED

< 1 month	< 1 year	< 5 years	> 5 years
11	17	16	42

TABLE III

THE EFFECT OF LUNG SCANS ON PRE-SCAN DIAGNOSIS

	Pre-scan diagnosis	Final diagnosis	No.
Refuting diagnosis	Bronchiectasis	Normal	3
	Inhaled foreign body	Normal	2
Establishing diagnosis	Hypertransradiant lung	Absent pulmonary artery	2
	Pulmonary emboli	Parenchymal lung disease	2
	Upper lobe consolidation	Congenital lobar emphysema	1

by the chest radiographs was also taken into account. The images were also scored by all the authors using a semi-quantitative scoring system (Fazio *et al.*, 1978), and a final decision about the significance of the findings and whether more invasive investigations were required was taken at a regular weekly meeting with the clinicians responsible for the patient's management, unless urgent decisions were required.

RESULTS

At least four view ventilation and perfusion scans were obtained in all children studied. Only two of the 100 scans were of poor quality.

Establishing or refuting a diagnosis (ten patients) (Table III)

Lung scans enabled a diagnosis to be confirmed or excluded in ten out of 86 children studied. In three children thought to have bronchiectasis, bronchograms were performed which confirmed the normal scan findings. In two children who were thought to have inhaled foreign bodies, chest fluoroscopy confirmed the normal scan findings, no further investigations being performed. In two children with unilateral hyperlucent lungs and absent ^{99}Tc^{m}MAA perfusion on the affected side, pulmonary angiography was performed to confirm the scan findings. Figure 1 shows the relevant investigations in one of these children. Three patients were referred for suspected pulmonary embolization and in two of these, matched ventilation and perfusion defects were found indicating parenchymal lung disease rather than pulmonary embolization, the findings on pulmonary embolization being a decrease in perfusion relative to ventilation in the affected area (McNeil, 1976). The scan of one of these patients is shown in Fig. 2.

In children with lobar emphysema the lung scan showed complete absence of ventilation and perfusion in the emphysematous areas. Usually these patients could be diagnosed on chest radiography and screening, but in one infant the diagnosis was changed from upper lobe collapse/consolidation because of the scan findings (Fig. 3).

Assessing the extent and regional distribution of the lung disease (81 patients)

When abnormal, lung scans adequately assessed the extent and the distribution of the lung pathology in all the patients studied, including those in Tables III and IV. In seven children with a proven diagnosis of bronchiectasis (five) or inhaled foreign body (two) the lung scan confirmed the site and extent of the damage demonstrated by bronchography, chest screening or bronchoscopy. Figure 4 shows the bronchographic findings performed at the referring

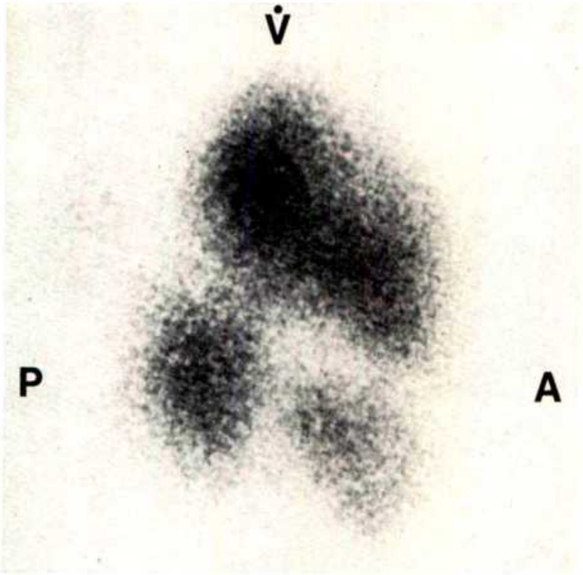


FIG. 5.

Right posterior oblique ventilation ($\dot{V}$) lung scan in a six-year-old with severe obliterative bronchiolitis, following an adenovirus pneumonia at the age of two years. Defects of ventilation are shown which approximate to the expected positions of the interlobar fissures. The perfusion scan showed similar features.

hospital alongside the lung scan. The areas of damage shown by bronchography show reduced perfusion and ventilation on the scans.

In the cystic fibrosis group (18 patients) seven were infants and 11 were children over three years. In the infants all except one had elevated thoracic gas volumes and markedly increased airways resistance, as measured in an infant plethysmograph, yet the only significant findings on the lung scans were small defects of both ventilation and perfusion in the centre of the lungs when the oblique projections were viewed. In the three older children with obliterative bronchiolitis who also had severe airflow obstruction and gas trapping, similar features were

TABLE IV

THE ASSESSMENT OF TREATMENT

Diagnosis	No. of patients
Aberrant left pulmonary artery	4
Absent left pulmonary artery	1
Cystic fibrosis	3
Foreign body (following removal)	1
Total	9

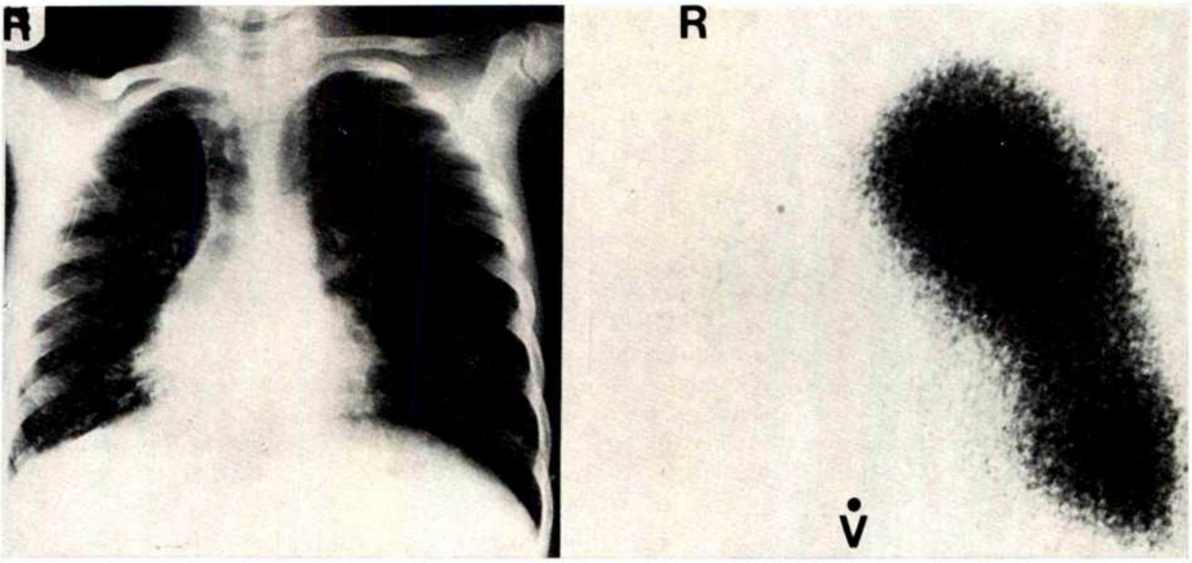


FIG. 6.

AP chest radiograph and the anterior ventilation ($\dot{V}$) lung scan in a seven-year-old boy with congenital icthyosis, basal bronchiectasis and bronchial lability. On auscultation his right lung had the same intensity of breath sounds as the left although it contained showers of fine crepitations. The radiograph shows a relative small right hemithorax with increased lung markings on the right and herniation of the left lung across the mid-line. The ventilation scan shows almost complete absence of radionuclide in the right lung. The perfusion scan showed similar features.

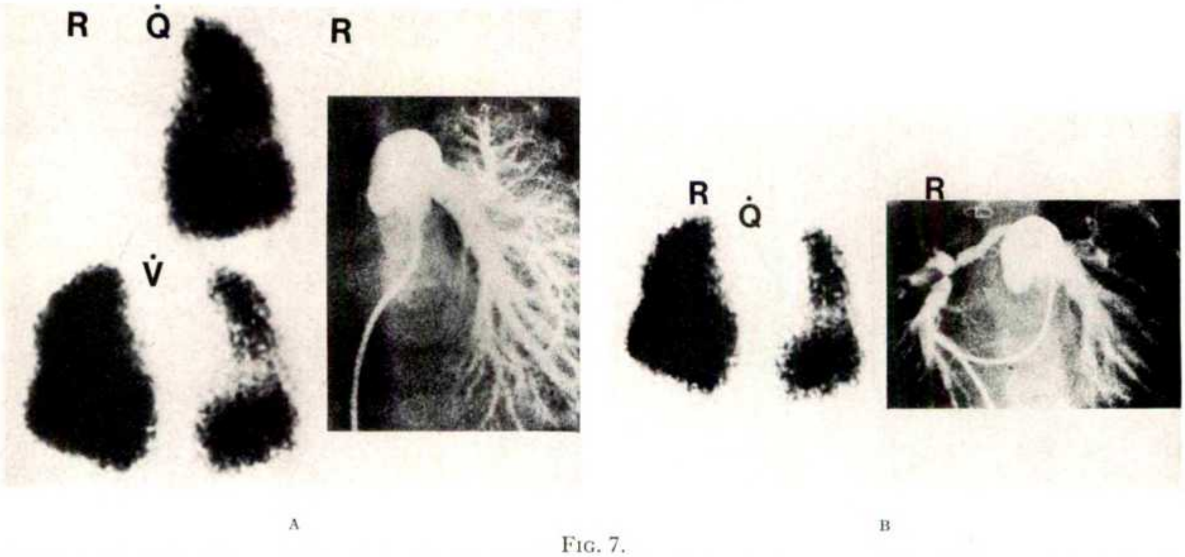


FIG. 7.

(A) Pre-operative anterior perfusion ($\dot{Q}$) and ventilation ($\dot{V}$) lung scans with the anterior view of the pulmonary angiogram in a four-week-old infant with a short segment right pulmonary artery atresia. The right lung shows normal ventilation with total absence of perfusion. The pulmonary angiogram confirms the congenitally absent right pulmonary artery.

(B) Post-operative anterior perfusion ($\dot{Q}$) lung scan and anterior pulmonary angiogram in the same infant. The lung scan reveals better perfusion of the right lung than the left with normal ventilation this is in spite of the relatively narrow appearances of the post-operative right pulmonary artery conduit.

also observed on lung scanning with defects of ventilation and perfusion in the regions of the interlobar fissures (Fig. 5).

In children with severe lung disease, extensive functional abnormalities could be detected on scanning which were not suspected on clinical or radiological grounds. Figure 6 shows the chest radiograph and the anterior lung scan in such a child.

The scans on three infants with unilateral pulmonary hypoplasia showed that in two, significant function was present in the affected lung where very little or none was thought possible on clinical or radiological grounds. Likewise six children with recurrent episodes of basal or middle lobe atelectasis were shown to have no residual or underlying abnormalities of ventilation or perfusion. In children with alveolitis or pulmonary fibrosis, the assessment of the extent of the functional involvement allowed the natural history of the disease to be followed as well as the response to therapeutic interventions.

The assessment of treatment (*nine patients*) (Table IV)

Lung scans were used in the post-operative assessment of four patients who had surgical correction of an aberrant left pulmonary artery causing upper airway obstruction. In each case a normal pulmonary circulation was demonstrated on the operated side. In one infant with a short-segment left pulmonary artery atresia a post-operative scan showed a pulmonary circulation to be present. His pre- and post-operative pulmonary angiograms and lung scans are shown in Fig. 7.

As far as medical therapy is concerned, changes in the distribution of ventilation and perfusion were observed after intensive courses of antibiotics and physiotherapy. In three children with cystic fibrosis, marked changes were noted in one child with moderate disease but less improvement was seen in two other children with very severe disease. Figure 8 shows the posterior ventilation lung scans in the child with moderate disease before and after such a course of treatment. This use of lung scans has been and is continuing to be applied to children with severe lung disease associated with alveolitis, fibrosis, or airflow obstruction when high dose steroid therapy is being given.

DISCUSSION

The ease with which $^{99}\text{Tc}^{\text{m}}$MAA $^{81}\text{Kr}^{\text{m}}$ radionuclide scans are performed and the high quality of the images obtained confirms the findings of Li and associates (1979). All lung scans reported here

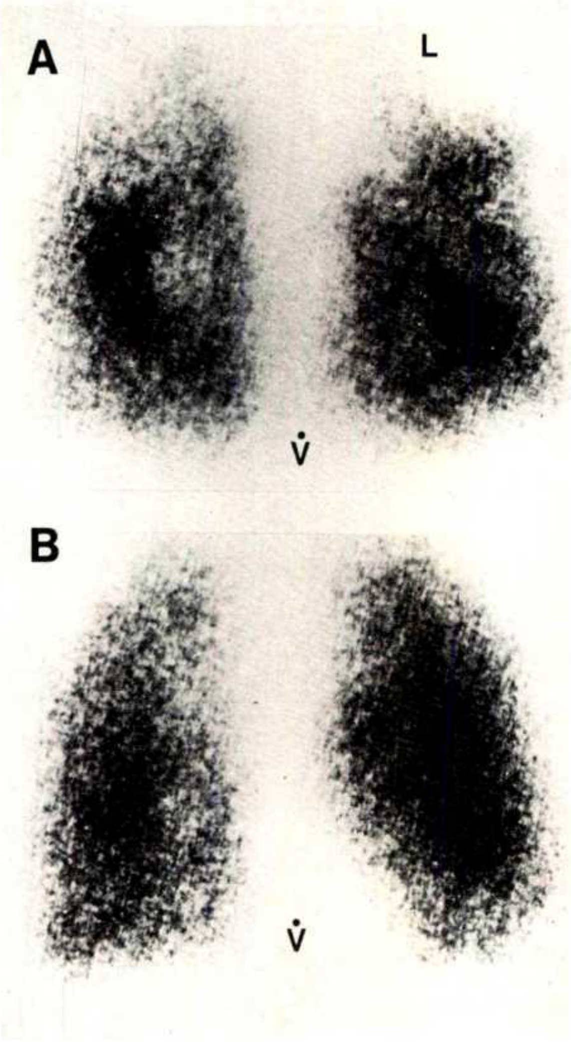


FIG. 8.

Anterior ventilation $(\dot{V})$ lung scans in a 12-year-old boy with cystic fibrosis. Scan A was performed at the beginning of a two week course of systemic antibiotics and intensive physiotherapy. Scan B is the post-treatment anterior view. Pulmonary function studies over the same period showed improvements in forced expired volumes and peak expiratory flow rate. The radiographs taken before and after the two week treatment were unchanged. The segmental defects were well matched on the perfusion scan and significant improvement is noted in the post treatment (B) scan.

were obtained in the supine position, mainly because with young children it had proved impracticable to maintain their co-operation for the 20 minutes necessary for a four-view set of studies in the erect position. For infants, all other investigations are performed in the same position, which is also their most commonly adopted one. In older children other investigations are performed in the upright position, and an assessment of the effect of posture on abnormal ventilation lung scans is currently being undertaken.

The steady state ventilation images of ^{81}Kr^{m} provide an index of regional ventilation in adults (Fazio and Jones, 1975) and in older children with a similar ratio of alveolar ventilation to unit lung volume the same conditions are operating. In infancy and early childhood a faster respiratory frequency results in a two- or threefold increase in alveolar ventilation per unit lung volume, and an equilibrium of inhaled radionuclide may be approached. Exactly how significant this effect becomes in infants and very young children is difficult to assess but it was interesting to observe the close matching of ventilation and perfusion defects in all age groups with parenchymal lung disease. This suggests that even in the youngest children the effective distribution of ventilation is still being seen with ^{81}Kr^{m}.

A number of second line imaging procedures is commonly being used for the diagnosis and assessment of children with lung disease. With the exception of chest fluoroscopy they are invasive techniques which carry an appreciable morbidity and all involve a higher radiation dose to the patient than a combined ^{99}Tc^{m}/^{81}Kr^{m} lung scan (Table V).

In ten of the 86 patients, the lung scan enabled a final diagnosis to be reached. In the presence of a

TABLE V

COMPARATIVE TARGET ORGAN RADIATION IN cGY (RAD)

	1 year	14 years
Chest radiograph PA and lateral	0.05	0.07
1.5 min fluoroscopy	1.2	3.3
^{99}Tc^{m} MAA lung scan	0.9	0.65
^{81}Kr^{m} lung scan	0.072	0.016
Cineradiography	2.8	10.6
Cardiac fluoroscopy (30 min)	24	66
Bronchography	12.2	33.3

Data sources

Chest radiograph, fluoroscopy and ^{99}Tc^{m} MAA lung scan: Webster *et al.* (1974). ^{81}Kr^{m}: Myers (personal communication). Cineradiography, cardiac fluoroscopy: Martin and Olson (1980). Bronchography: Hospital for Sick Children calculations. (Fluoroscopy was performed with image intensification and manually variable kV (50 to 110) with automatic mA.)

normal scan there is little likelihood of any significant disease being present. This has been of great value in children who have inhaled foreign bodies in the past and in children in whom bronchiectasis is strongly suspected. The opportunity afforded by perfusion lung scanning to evaluate the patency of a pulmonary artery without the need to resort to cardiac catheterization must be stressed. Since many children with aberrant left pulmonary arteries suffer from localized bronchomalacia there is also a need to carry out a ventilation scan.

In assessing the regional distribution and extent of the lung disease the combined $^{99}Tc^m$ MAA/$^{81}Kr^m$ scan is proving invaluable. It provides information unobtainable by other imaging techniques or by overall pulmonary function studies and also has the advantage that it can be used at any age with the same quality of images being obtained. With a standard four-view perfusion/ventilation lung scan most of the segments of each lobe can be well seen and if anterior oblique views are also performed for better visualization of the middle lobe and lingula the function of all the lobar segments can be accurately assessed. When this information is taken together with the chest radiograph, an anatomical and pathophysiological understanding of the disease process can be obtained. The contribution of lung scans to this understanding is well illustrated by the findings of decreased areas of ventilation and perfusion in the centre of the oblique projections in the infants with cystic fibrosis with significant airflow obstruction and gas trapping. These defects could be interpreted as the first development of "fissure signs" previously noted by others in older children with severe chest symptoms (Alderson *et al.*, 1974). In our population these "fissure signs" were most marked in children in the obliterative bronchiolitis group (Fig. 5). In the presence of severe small airways disease any resultant ventilation defects would be expected to become more apparent at the junction of lung lobes. Care should be taken in interpreting the lung scan when bronchial lability complicates parenchymal lung disease, as large matched defects of ventilation and perfusion are often seen in the presence of airflow obstruction. These defects can be significantly improved or eradicated with bronchodilators (Fazio *et al.*, 1979). By performing lung function studies in which bronchial lability is looked for, or by repeating the ventilation lung scan after treatment with bronchodilators, this potential difficulty can be overcome.

Regarding the assessment of treatment in those children who have had pulmonary vascular surgery, a post-operative ventilation/perfusion scan is the only non-invasive accurate assessment of the effect of that surgery (Dunn *et al.*, 1979.) In the children with cystic fibrosis, repeat scans after intensive courses of physiotherapy and systemic antibiotics have shown improvements in the distribution of perfusion and ventilation with little change on chest radiography. Further studies in this application of lung scans to appraise present treatment strategies are currently being undertaken.

ACKNOWLEDGMENTS

We thank Dr. D. Matthew and Dr. R. Dinwiddie of the Respiratory Unit and all the physicians and surgeons of the Hospital for Sick Children who have referred their patients for lung scanning. The Medical Research Council Cyclotron Unit at the Hammersmith Hospital London provided the $^{81}Kr^m$ generators. Dr. P. Helms was supported by the Medical Research Council.

REFERENCES

ALDERSON, P. O., SECKER WALKER, R. H., STROMINGER, D. B., MCALISTER, W. H., HILL, R. L. and MARKHAM, J., 1974. Quantitative assessment of regional ventilation and perfusion in children with cystic fibrosis. *Radiology, 111*, 151–155.

CHANDRA, R., SHAMOUN, J., BRAUNSTEIN, P. and DUHOV, O. L., 1973. Clinical evaluation of an instant kit for preparation of ^{99m}Tc MAA for lung scanning. *Journal of Nuclear Medicine, 14*, 702–705.

CLARK, J. C., HORLOCK, P. L. and WATSON, I. A., 1976. Krypton 81m generators. *Radio-chemical and Radio-analytical Letters, 25*, 245–254.

COGSWELL, J. J., 1973. Forced oscillation technique for determination of resistance to breathing in children. *Archives of Disease in Childhood, 48*, 259–266.

DAB, I. and ALEXANDER, F., 1976. A simplified approach to the measurement of specific airway resistance. *Pediatric Research, 10*, 996–999.

DUNN, J. M., GORDON, I., CHRISPIN, A. R., DELEVAL, M. R. and STARK, J., 1979. Early and late results of surgical correction of pulmonary artery sling. *Annals of Thoracic Surgery, 28*, 230–238.

FAZIO, F. and JONES, T., 1975. Assessment of regional ventilation by continuous inhalation of radioactive krypton 81m. *British Medical Journal*, 673–676.

FAZIO, F., LAVENDER, J. P. and STEINER, R. E., 1978. ^{81m}Kr ventilation and ^{99m}Tc perfusion scans in chest disease: comparison with standard radiographs. *American Journal of Radiology, 130*, 421–428.

FAZIO, F., PALLA, A., SANTOLICANDRO, A., SOFANELLI, S., FORNAI, E. and GIUNTINI, C., 1979. Studies of regional ventilation in asthma using ^{81m}Kr. *Lung, 156*, 185–194.

GODFREY, S. and MCKENZIE, S., 1977. The place of radio-isotope lung function studies in paediatrics. *Archives of Disease in Childhood, 52*, 859–864.

KNIPPING, H. W., BOLT, W., VENRATH, H., VELENTIN, H., CUDES, H. and ENDLER, P., 1955. Eine neue Methode zur Prüfung der Herz- und Lungenfunktion. *Deutsche Medizinische Wochenschrift, 80*, 1146–1147.

LI, D. K., TREVES, S., HEYMAN, S., KIRKPATRICK, J. A. LAMBRECHT, R. M., RUTH, T. J. and WOLF, A. P., 1979. Krypton 81m: a better radiopharmaceutical for assessment of regional lung function in children. *Radiology, 130*, 741–747.

MCNEIL, B. J., 1976. A diagnostic strategy using ventilation-perfusion studies in patients suspect for pulmonary embolism. *Journal of Nuclear Medicine, 17*, 613–616.

MANSELL, A., LEVISON, H., KRUGER, K. and TRIPP, T. L., 1972. Measurement of respiratory resistance in children by forced oscillations. *American Review of Respiratory Disease, 106*, 710–714.

Martin, E. C. and Olson, A., 1980. Radiation exposure to the paediatric patient from cardiac catheterisation and angiography. *British Journal of Radiology*, *53*, 100–106.

Treves, S., Ahnberg, D. S., Laguarda, R. and Strieder, D. J., 1974. Radionuclide evaluation of regional lung function in children. *Journal of Nuclear Medicine*, *15*, 582–587.

Webster, E. W., Alpert, N. M. and Brounell, G. L., 1974. Radiation doses in paediatric nuclear medicine and diagnostic X-ray procedures. In: *Paediatric Nuclear Medicine* (W. B. Saunders, Philadelphia).

Williams, S. P., Fullton, J. M., Tsai, M. J., Pimmel, R. L. and Collier, A. M., 1979. Respiratory impedance and derived parameters in young children by forced random noise. *Journal of Applied Physiology*, *47*, 169–174.

Book reviews

Nuclear Medicine Examination Review. By G. D. Frey and C. J. Klobukowski. 2nd ed. 366 pp. 1980. (Medical Examination Publishing Co., New York), £14·50.
ISBN 0-87488-457-8

The 1425 multiple-choice questions in this book deal with all aspects of nuclear medicine, including *in vitro* procedures and therapy. Eleven of the chapters deal with the clinical aspects, including relevant physiology, whilst the remaining 13 cover the basic sciences (physics, radiobiology etc.), instrumentation, radiopharmaceuticals, safety and quality control. Most of the questions have four or five alternative answers but some are of the form where the reader has to decide whether a statement is true or false. The reader is referred at the end of each question to a page in one of the 51 references listed for further information. The answers are all printed together at the end of the book.

The book is aimed at the nuclear medicine technologist and is suitable for radiographers, medical physics technicians and others entering the field of nuclear medicine. However, the British reader will find the emphasis and choice of questions strange in places; little attempt has been made to accommodate the non-American reader. The difference in techniques and practice is understandable; indeed it can be beneficial in causing the reader to be more critical of familiar practices. The lack of inclusion of any mention of $^{81}\mathrm{Kr}^{\mathrm{m}}$ is a significant omission and the emphasis on radionuclide techniques for placental studies is misleading. There are other questions which challenge the claim that this second edition is completely revised—too much of it reflects procedures current at the time of the first edition.

The failure to use SI units is a positive disadvantage—as is, to a lesser degree, the lack of mention of computers in the instrumentation section.

The questions are well phrased and in general the alternative answers provided are discriminating. A book which would be a useful addition to a departmental library and best used in tutorials where guidance is available for the student.

P. H. S. Smith.

Nuclear Medicine: Hepatolienal. Ed. by B. Rothfeld, pp. xi+255, 1980 (Harper & Row, London), £29·25.
ISBN 397-5041-28

This book is unique in that, for the first time, most aspects of nuclear medicine in relation to the liver and spleen are drawn together between two covers. As the editor states, technical details are kept to a minimum whereas the basic principles of the tests involved, their indications and interpretations are emphasized. It begins with a useful review of the anatomical variations of the normal liver followed by chapters on reticuloendothelial cell and parenchymal cell localizing agents, scintiangiography, imaging of hepatic abscesses and trauma, and hepatic neoplasms. The next three chapters are all devoted to viral hepatitis antigens, and then a section on bile acids, α-fetoprotein, and carcinoembryonic antigen follows. Although of interest, the space devoted to these subjects with only limited connections with nuclear medicine seems excessive. The book ends with contributions on radioactive breath tests, splenic imaging and splenic function.

The black-and-white illustrations are clear, with comprehensible though lengthy legends. The book is aimed at "internists, clinical pathologists, radiologists and gastroenterologists," rather than at nuclear physicists. Since it is the first of its kind, it should be on the shelves of nuclear medicine departments for easy reference, but specialists in this field may not feel so inclined to purchase it for themselves as so much of the content is either already well known or not strictly relevant to nuclear medicine.

James Marigold,
Desmond Croft.

1981, *British Journal of Radiology*, *54*, 586–591

Radionuclide section scanning of the lungs in pulmonary embolism

By O. Khan, B.Sc., Ph.D.(Lond.), M.B., B.S., P. J. Ell, M.D., M.Sc., P. H. Jarritt, B.Sc., Ph.D., I. Cullum, M.Sc., and E. S. Williams, M.D., Ph.D., F.R.C.P.

Institute of Nuclear Medicine, Middlesex Hospital Medical School, London W1

(Received November 1980 and in revised form March 1981)

ABSTRACT

A new approach to the radionuclide imaging of the lungs is illustrated in this paper, describing four patients who were subjected to section scanning of the chest in addition to conventional planar imaging.

The significance of this new method in the investigation of patients suspected of having pulmonary embolism is discussed. The main advantages of the new approach include increased information with depth, clearer definition of the mediastinal space, and the detection in some instances of new lesions not seen by conventional means.

Despite its drawbacks, radionuclide scanning still remains an important investigation in the detection of pulmonary embolism (Neumann *et al.*, 1980). One such drawback concerns the sensitivity of the procedure which requires multiple views of the lungs if defects deep within its substance are to be visualized. Even with multiple views, however, the scan may not always reflect accurately the significance or the degree of a partially occluded lung segment (Moser *et al.*, 1969). This problem is partially explained by the fact that the lungs are large three-dimensional organs which cannot be adequately visualized with conventional two-dimensional views alone.

The inherent disadvantage of conventional imaging is that information which arises from different planes of an organ to be scanned is superimposed on the same plane in the final displayed image, resulting in loss of contrast and hence in clinical information. Radionuclide section scanning has been shown to offer extra sensitivity and greater accuracy in the localization and definition of lesions in the brain (Ell *et al.*, 1980a), liver (Ell *et al.*, 1980b) and heart (Donaldson *et al.*, 1980) when compared with conventional gamma-camera imaging. It was therefore decided to extend this new imaging technique to the lungs in order to investigate any possible advantages which emission tomography might offer in the detection of pulmonary embolism.

PATIENTS AND METHODS

Four patients with suspected pulmonary embolism were investigated by standard methods including chest radiography and ECG. In some cases, X-ray phlebography and the ^{99}Tc^{m}-plasmin uptake test (Deacon *et al.*, 1980) were performed in those patients with suspected deep vein thrombosis (DVT).

^{133}Xe gas was used for the initial ventilation study and a standard protocol was followed. After the ventilation scan, perfusion scans were obtained ten min after intravenous injection of 150 MBq (4 mCi) of ^{99}Tc^{m}-labelled macroaggregated albumin. Six conventional views with 400000 counts (anterior, posterior, right and left lateral and right and left posterior oblique) were obtained with a large field of view gamma camera (Digicamera, Scintag Berthold).

Radionuclide section scans of the lungs were recorded immediately after the perfusion study, using a Cleon-711 whole-body emission tomographic scanner. Figures of merit for this instrument have been published recently (Jarritt and Ell, 1980).

With the Cleon-711 scanner, scanning was commenced at the base of the neck so as to avoid missing the apices of the lungs, and continued for at least one further slice when the diaphragm was reached. Usually eight tomographic slices were obtained with an acquisition time of 5 min per slice. The thickness of each slice was 2.5 cm with identical spacing.

RESULTS

Case 1

A 21-year-old female who had been on oral contraceptives for the past three years complained of intermittent haemoptysis over this period. She had no chest pain or shortness of breath. A bronchial adenoma was suspected but bronchoscopy was reported as normal. Her chest radiograph and a ventilation/perfusion scan (Fig. 1A) were reported as normal. Tomographic section scans (Fig. 1B) confirmed the absence of perfusion defects. In sections 5, 6 and 7, which represent sections taken at the base of the lungs, the cardiac impression on the left lung is shown rather well. In addition, a well-defined area of reduced radioactivity (arrowed) in the right lung which corresponds to the dome of the right hemidiaphragm is seen.

Case 2

A 39-year-old female with pain and swelling of her left calf complained of a two-weeks' history of left-sided pleuritic chest pain associated with progressive shortness of breath but no haemoptysis. With two recent episodes of these symptoms, a diagnosis of recurrent pulmonary embolism was suspected, for which a ventilation/perfusion scan was requested.

Her chest radiograph showed shadowing of the right base and slight elevation of the right hemidiaphragm. The rest of

---

Reprint requests: Dr. P. J. Ell.

the lung fields were clear. X-ray phlebography and a ^{99}Tc^{m}-plasmin uptake study confirmed the presence of bilateral DVT. Whilst the ventilation scan was normal, segmental perfusion defects affecting the upper and lower zones of both lungs were seen (Fig. 2A).

The pulmonary transverse section scans (Fig. 2B) agreed well with the findings of the conventional study. Multiple but superiorly defined perfusion defects can be recognized in each of the selected tomographic slices.

Pulmonary arteriography performed two days later at the hospital of her referral was reported as showing an occluded segment in the right lower zone, a second segment in the left upper zone and probably some interruption in the vessels supplying the left lower lobe (Fig. 2C).

Case 3

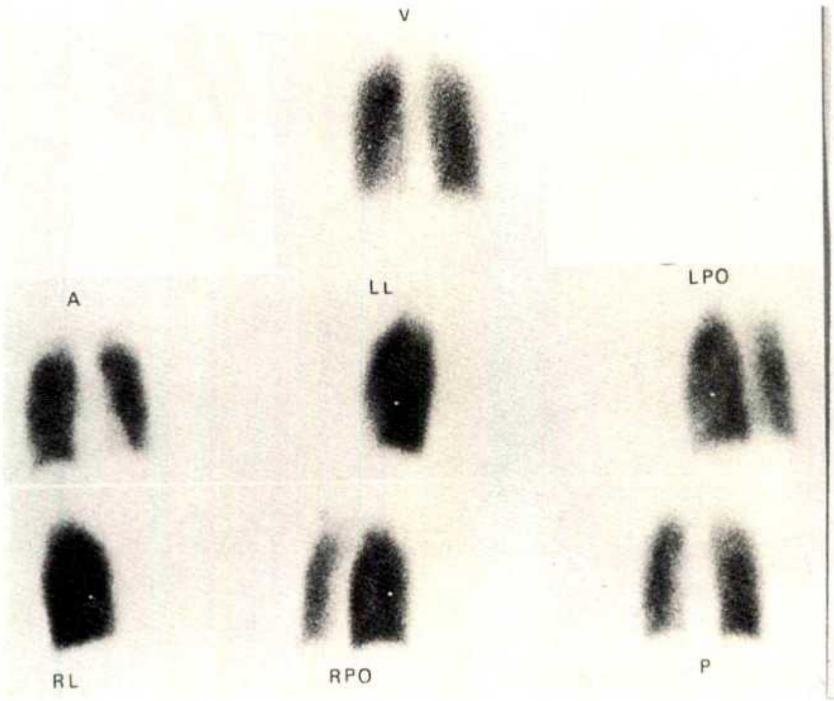
This case concerns an 80-year-old female admitted as an emergency with sudden onset of shortness of breath ascribed initially to left ventricular failure. Despite rigorous medical treatment, her shortness of breath persisted, for which she was referred for a lung scan.

Whilst the ventilation study was normal, widespread segmental perfusion defects affecting both lungs were noted (Fig. 3A). The tomographic section scans (Fig. 3B) (selected sections only) provided a more dramatic representation of the extent of hypoperfusion in the upper zone and the base of the right lung.

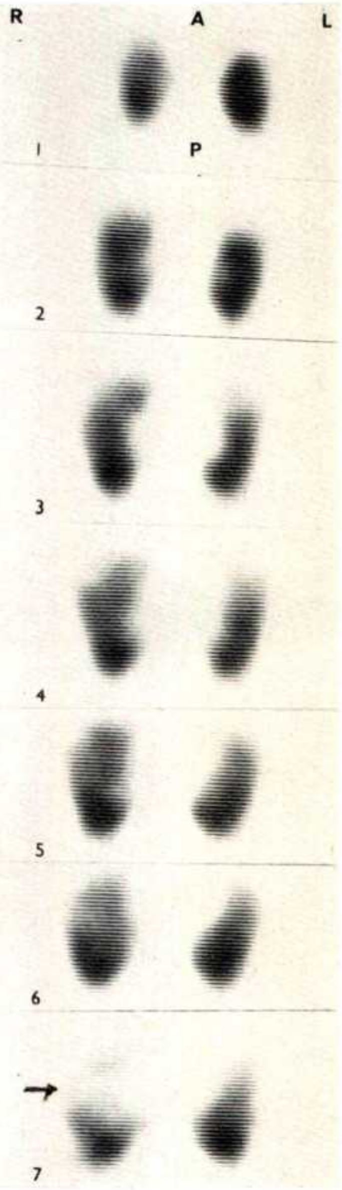
Two weeks following heparinization, she was clinically much improved. A repeat ventilation/perfusion scan (Fig. 3C) confirmed the significant improvement in perfusion of both lungs, although with remaining evidence of widespread embolic disease. Repeat emission tomographic scans (Fig. 3D) showed marked improvement in perfusion to the upper zone of the right lung but revealed in addition widespread involvement of the middle and lower zones of the left lung, which were not as evident on the conventional views.

Case 4

A 50-year-old woman who presented with right sided pleuritic chest pain only, with suspicion of having pulmonary embolism, was referred for a lung scan. Her chest radiograph and ventilation studies were normal, as was the clinical examination.



A



B

Fig. 1.

(A) Normal ventilation (V) and perfusion scan (six views). Conventional planar imaging with the gamma camera.

(B) Transverse section scans (from apex-1 to base-7) of the perfusion of the lungs of the same patient are shown. Note in section 7 the arrowed pseudo defect caused by the dome of the right diaphragm.

Whilst the perfusion scan appeared to be essentially normal (Fig. 4A), the emission tomography study (Fig. 4B, sections 5 and 6) demonstrated the unequivocal presence of a large defect in the right lung not detected by the conventional study.

DISCUSSION

In the cases which we have described, radionuclide section scanning of the lung permitted a display of the entire lung volume with substantial improvement in image contrast and information with depth. These improvements led in Cases 2 and 3 to better visualization of segmental defects and in Case 4 to the detection of defects not seen by the conventional two-dimensional scan. This is not surprising, since the visualization of defects in a large organ such

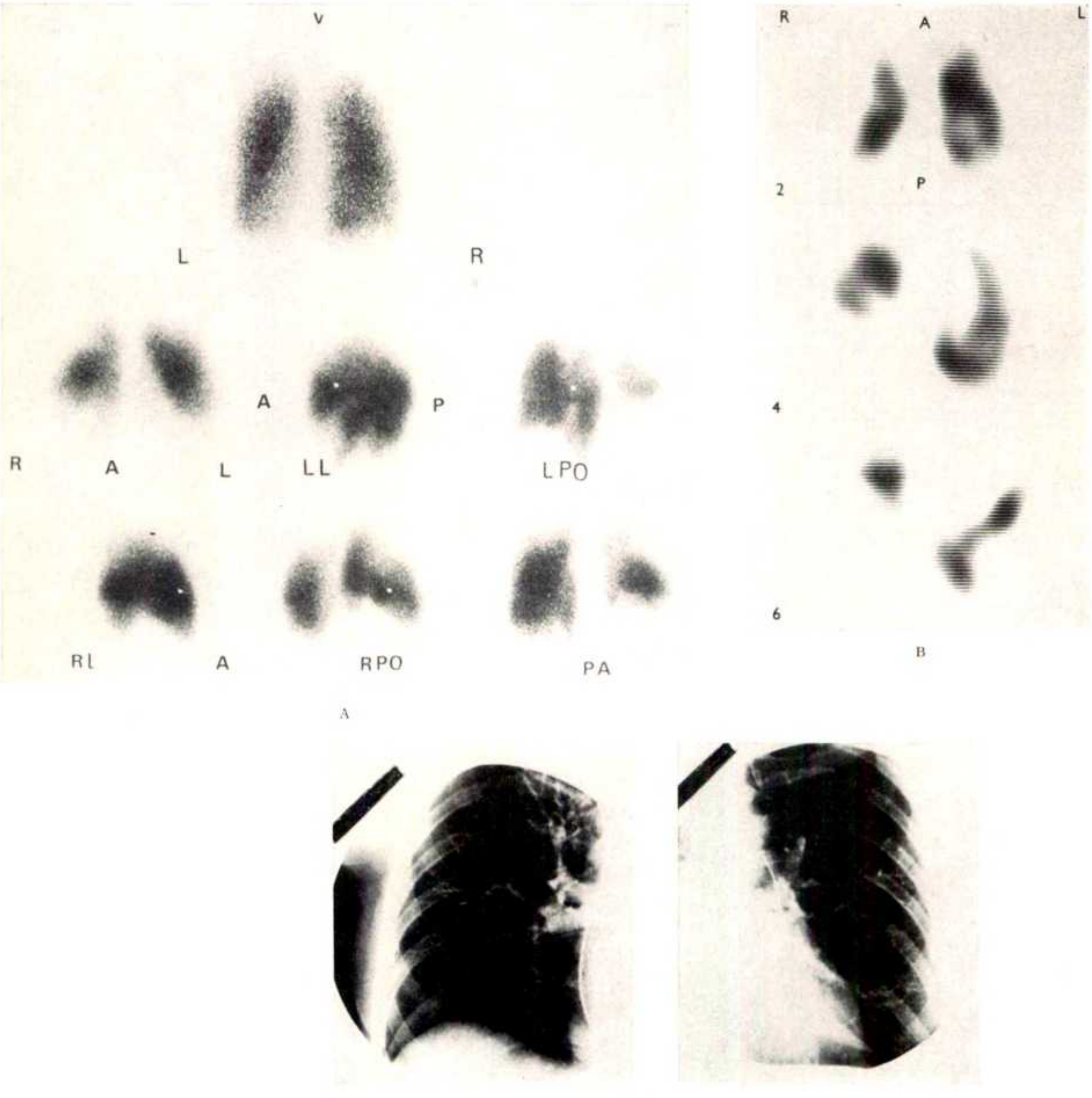
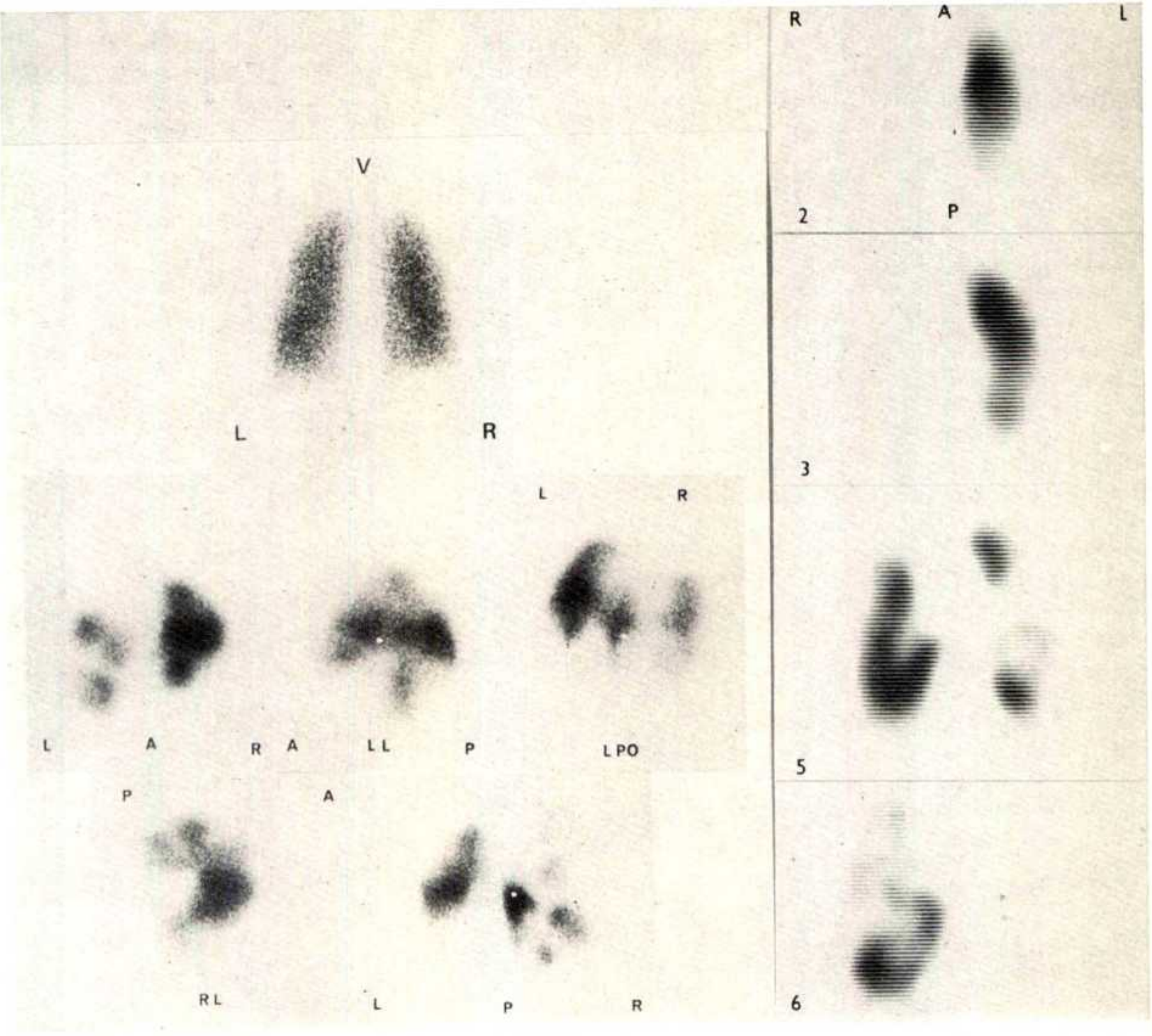


FIG. 2.

(A) A normal ventilation scan (V) and the six perfusion scans of a patient with suspected embolic lung disease. Note the abnormal perfusion pattern in the upper and lower zones of both lungs.

(B) Transverse section scans of the perfusion of the lungs of the same patient. Note the superior definition of the perfusion impairment, also partially seen in the pulmonary angiogram (C).



A FIG. 3. B

(A) Normal ventilation scan (V) and multiple perfusion defects affecting both lungs (before therapy).

(B) Corresponding transverse section scans. Note extensive involvement of both lungs, in particular the absence of significant perfusion to the upper zone of the right lung.

as the lungs is rendered difficult if only two-dimensional planar projections are obtained. With lesions situated deep in the substance of the lungs, the obvious danger is that these can be missed altogether.

Ventilation/perfusion lung scanning, despite its limitations, still remains the mainstay in the diagnosis of pulmonary embolism. A more objective method of definitively demonstrating the presence of pulmonary emboli is through pulmonary arteriography. This method has been shown to substantiate the findings of perfusion lung scans and excels in the detailed display of the major pulmonary vascular anatomy (Moses *et al.*, 1974). Its specialized nature and the risks of mortality and morbidity, however, preclude it as a suitable screening procedure.

In Case 2, substantial agreement was noted between pulmonary angiography and radionuclide section scanning. As angiography is still used as the reference procedure for the demonstration of pulmonary emboli, the results of this case suggest that emission tomographic section scanning of the lungs can be used as a valid, non-invasive alternative approach. Further comparative studies are currently in progress to investigate the validity of the tomographic technique.

Isotope section scanning appears also to be helpful when sequential lung scanning is performed in order to evaluate the efficacy of medical treatment. In Case 3 the planar images both before and after heparin therapy appeared to underestimate significantly the degree of hypoperfused lung tissue, and a better appreciation of lung involvement was obtained from emission tomography.

One area which might lead to difficulty in interpreting the section scans is the base of the right lung where the dome of the diaphragm may produce a "pseudo" defect. This defect is readily distinguishable from a true perfusion defect by its uniform shape and its position, and with practice it can be easily recognized.

Radionuclide section scanning promises to hold an interesting future in the detection of pulmonary embolic disease. Work is in progress with this technique in order to measure lung and mediastinal volumes; it is hoped that this might lead to a quantitative and more objective assessment of embolic disease including its response to therapy.

With multi-plane section imaging of the lungs, greater accuracy and sensitivity in lesion detection is to be expected. Further clinical work is however required to ascertain its ultimate role.

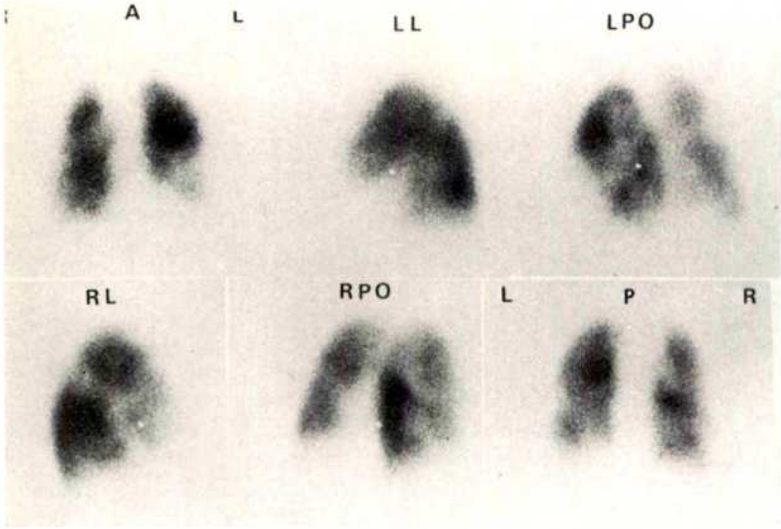
REFERENCES

DEACON, J. M., ELL, P. J., ANDERSON, P. and KHAN, O., 1980. Technetium ^{99m} plasmin—a new test for the detection of deep vein thrombosis. *British Journal of Radiology*, *53*, 673–677.

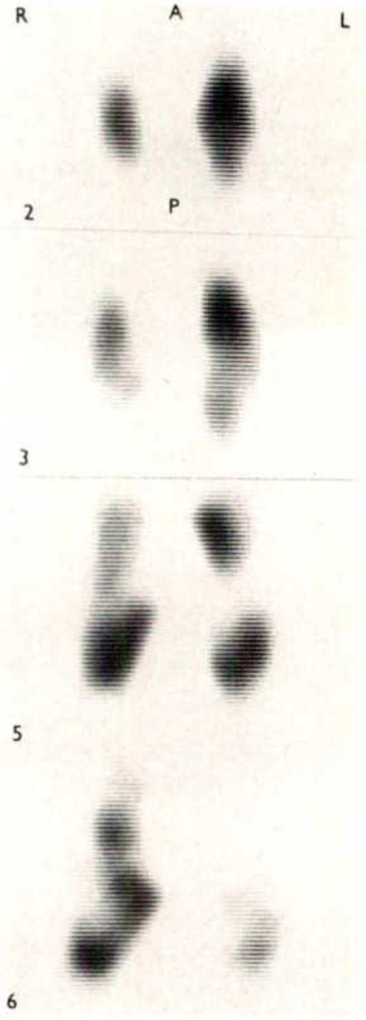
DONALDSON, R., ELL, P. J. and EMANUEL, R., 1980. ECT in acute myocardial infarction. *British Heart Journal*, *43*, 107.

ELL, P. J., DEACON, J. M., DUCASSOU, D. and BRENDEL, A., 1980a. Emission and transmission brain tomography. *British Medical Journal*, *60*, 438–444.

ELL, P. J., KHAN, O. and WILLIAMS, E. S., 1980b. The management of disease and radionuclide section scanning. *British Journal of Hospital Medicine*, *24*, 225–231.



C



D

FIG. 3.

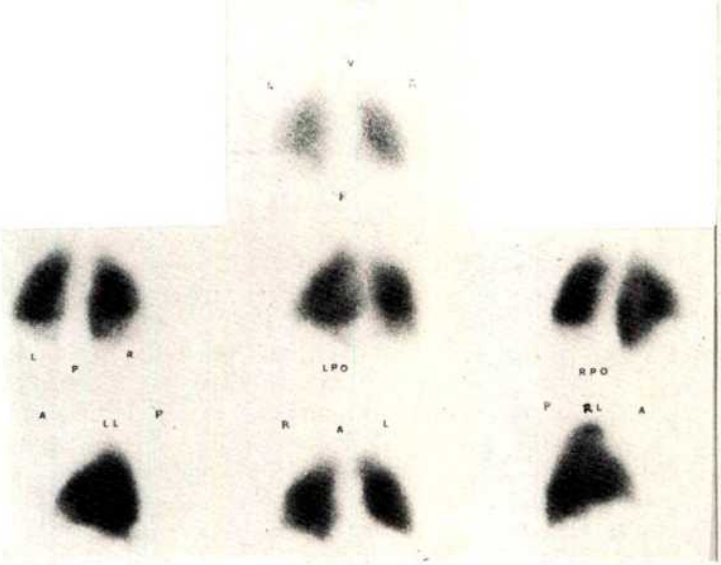
Repeat study two weeks later (after therapy). Note marked improvement. Striking reperfusion of the upper zone of the right lobe.

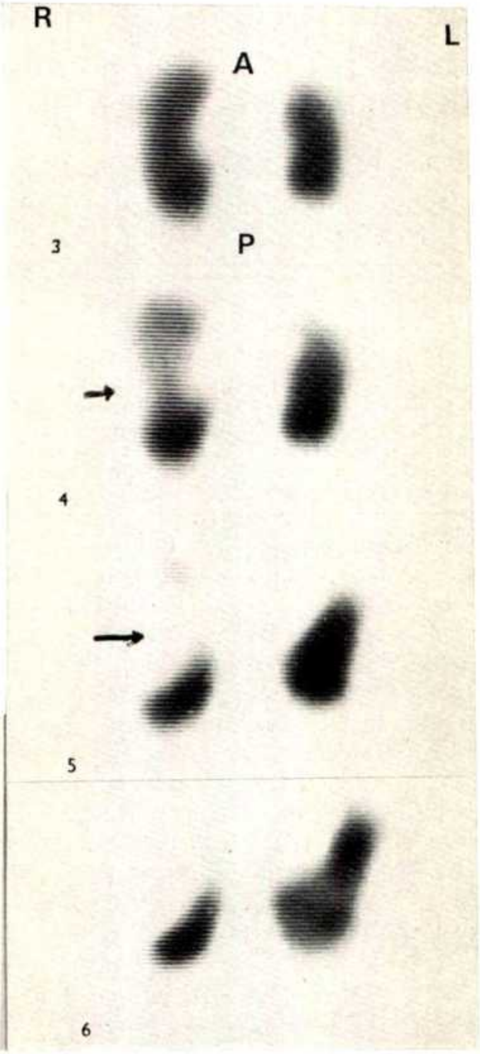
JARRITT, P. H. and ELL, P. J., 1980. A new emission tomographic body scanner. *Nuclear Medicine Communications*, *1*, 94–101.

MOSER, K. M., HARSANYI, P., RINS, G., GUISAN, J., LANDIS, G. A. and MIALE, A., JR., 1969. Assessment of pulmonary photoscanning and angiography in experimental pulmonary embolism. *Circulation*, *39*, 663.

MOSES, D. C., SILVER, T. M. and BOOKSTEIN, J. J., 1974. The complementary roles of chest radiography, lung scanning, and selective pulmonary angiography in the diagnosis of pulmonary embolism. *Circulation*, *49*, 179–188.

NEUMANN, R. D., SOSTMAN, H. D. and GOTTSCHALK, A., 1980. Current status of ventilation-perfusion imaging. *Seminars in Nuclear Medicine*, *10*, 198–217.





A FIG. 4. B

(A) Normal ventilation scan (V) and perfusion scan. Conventional study.

(B) Transverse section scans of the perfusion of the lungs. Note marked defects in sections 5 and 6.

1981, *British Journal of Radiology*, *54*, 592–596

Effects of acute administration of ethane hydroxydiphosphonate (EHDP) on skeletal scintigraphy with technetium-99m methylene diphosphonic acid (Tc-MDP) in the rat

By Iain Watt, M.R.C.P., F.R.C.R. and Penny Hill, Ph.D., B.Pharm., M.P.S.

Departments of Radiodiagnosis and Radiopharmacy, Bristol and Weston Health District (Teaching),
Bristol BS2 8HW

(*Received September 1980 and in revised form January 1981*)

ABSTRACT

A study has been performed in the rat to assess the effect of EHDP on the distribution of ^{99}Tc^{m}-labelled MDP used for skeletal imaging. Profound alterations in bone, kidney and blood levels were observed. These observations cast doubt on the value of bone scans for monitoring the therapeutic effect of diphosphonates.

The diphosphonates are a group of largely unmetabolized compounds, containing P–C–P bonds, which have become most familiar to radiologists as bone-seeking agents in skeletal imaging. Their uses are far more extensive (Russell and Fleisch, 1976), including the prevention of furring in cold water pipes, dental caries, the management of Paget's disease (Smith *et al.*, 1971; Lentle *et al.*, 1976; Meunier *et al.*, 1979; Murphy *et al.*, 1980) and myositis ossificans progressiva (Hentzer *et al.*, 1978). The diphosphonates impede the transformation of amorphous calcium phosphate into hydroxyapatite (Francis, 1969; Francis *et al.*, 1969) and block the aggregation of hydroxyapatite crystals.

Skeletal imaging with P–C–P agents is used also to diagnose and assess progress of Paget's disease (Miller *et al.*, 1974; Lentle *et al.*, 1976; Murphy *et al.*, 1980) and myositis ossificans (Suziki *et al.*, 1974). As P–C–P compounds are used both in diagnosis and treatment, changes in the scans may be due either to therapeutic improvement or to changes in pharmacological distribution that are unrelated to therapeutic effect. If the scans are to have any value in assessing progress, the progress needs to be measured. Accordingly a study has been undertaken in the rat to evaluate the effect of administering a therapeutic dose of EHDP before, with, and after the administration of ^{99}Tc^{m}-MDP for skeletal imaging.

MATERIALS AND METHODS

Adult male hooded rats between 250 and 320 g in weight were anaesthetized using intraperitoneal urethane, a dose of 1 g/kg body weight, following ether induction. Venous catheterization was achieved either by a tail vein puncture or by jugular dissection. Tracheostomy tubes were routinely inserted. The penis was ligated to prevent loss of urine following induction. Skeletal imaging was achieved using freshly made ^{99}Tc^{m}-labelled MDP at an activity comparable to that used in humans (7.4 MBq/kg). Normal values of tissue distribution were obtained in groups of at least five animals at one, two, three and four hours from injection of Tc-MDP. EHDP was administered intravenously to further groups at a dose of 20 mg/kg at different timings from the administration of Tc-MDP. The intravenous route was selected because of considerable variability of oral absorption in experimental animals (Michael *et al.*, 1972). Groups were studied with injection of EHDP two hours before Tc-MDP (−2 EHDP), one hour before (−1 EHDP), concurrently (0 EHDP), and one and two hours after Tc-MDP (+1 and +2 EHDP). Groups were killed one, two, three and in some circumstances four hours after the administration of Tc-MDP. Scintigrams of the animals before killing were obtained using a gamma camera. At the completion of each experiment, activity levels were estimated from blood, muscle, the whole urinary bladder, and from kidney and the femora. All specimens were fragmented to obtain a uniform geometry and activity was estimated in a well counter with reference to a standard injection. Chromatographic quality control was performed on the Tc-MDP and in no case was more than 2% of the technetium compound unlabelled. Tissue levels were expressed in percentage of administered dose in each gram of tissue.

In order to assess whether observed changes were dose-dependent, groups of animals were injected with either 5, 10 or 20 mg/kg of EHDP one hour before Tc-MDP and killed one hour later. A control group was studied following injections of saline.

RESULTS

The experimental animals proved to be extremely sensitive to the rapid injection of EHDP and about one in ten died. Death was characterized by tetany and respiratory paresis together with electrocardiographic changes consistent with hypocalcaemia or hyperkalaemia. No difficulty was encountered with slow injection over two to three minutes.

Control animals (*Tables I-VI*)

Bone levels did not vary significantly over the one to four hour period. Renal activity was shown to decline against time ($p < 0.001$) and renal activity correlated with a change in renal size ($p < 0.05$). Blood levels were also shown to decline against time ($p < 0.001$). There was a strong correlation between kidney and blood levels ($p < 0.001$) and between bone and blood levels at one hour ($p < 0.001$). However, there was no correlation between these levels throughout the whole four hour period. Urinary

TABLE I

Bone levels percent/g

	1 hour	2 hours	3 hours	4 hours
Control	1.84 ± 0.10	1.46 ± 0.10	1.77 ± 0.08	1.42 ± 0.06
EHDP − 2 h	0.92 ± 0.08***	1.29 ± 0.09*	1.28 ± 0.09**	—
EHDP − 1 h	1.02 ± 0.08***	1.58 ± 0.12	1.49 ± 0.19	—
EHDP with MDP	0.91 ± 0.07***	1.41 ± 0.05	1.63 ± 0.08	1.75 ± 0.09*
EHDP + 1 h	—	1.77 ± 0.20	1.36 ± 0.05**	1.72 ± 0.04**
EHDP + 2 h	—	—	1.39 ± 0.07**	—

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

TABLE II

Kidney level percent/g

	1 hour	2 hours	3 hours	4 hours
Control	6.34 ± 0.80	4.89 ± 0.69	1.90 ± 0.44	1.04 ± 0.26
EHDP − 2 h	11.49 ± 1.09**	8.53 ± 1.27	9.42 ± 2.22*	—
EHDP − 1 h	13.96 ± 1.35***	14.59 ± 2.99**	9.35 ± 2.55*	—
EHDP with MDP	11.64 ± 3.09	16.70 ± 2.70**	14.74 ± 2.09***	13.86 ± 2.20***
EHDP + 1 h	—	7.23 ± 0.77*	3.03 ± 0.54	2.85 ± 0.84
EHDP + 2 h	—	—	2.48 ± 0.59	—

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

TABLE III

Blood levels percent/g

	1 hour	2 hours	3 hours	4 hours
Control	0.20 ± 0.04	0.10 ± 0.02	0.08 ± 0.00	0.04 ± 0.00
EHDP − 2 h	0.28 ± 0.02*	0.19 ± 0.02**	0.12 ± 0.01*	—
EHDP − 1 h	0.30 ± 0.04*	0.19 ± 0.02*	0.11 ± 0.02	—
EHDP with MDP	0.23 ± 0.01	0.20 ± 0.01***	0.11 ± 0.01	0.11 ± 0.01***
EHDP + 1 h	—	0.28 ± 0.04**	0.09 ± 0.01	0.09 ± 0.01***
EHDP + 2 h	—	—	0.09 ± 0.02	—

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

TABLE IV

Bladder percent total dose

	1 hour	2 hours	3 hours	4 hours
Control	20.72 ± 6.50	28.47 ± 6.32	44.20 ± 4.24	63.76 ± 4.24
EHDP − 2 h	11.43 ± 4.76	35.54 ± 7.52	37.46 ± 11.22	—
EHDP − 1 h	4.77 ± 3.33*	14.57 ± 6.83	40.91 ± 10.20	—
EHDP with MDP	13.66 ± 7.58	8.43 ± 5.38*	20.61 ± 5.43**	24.32 ± 6.24***
EHDP + 1 h	—	9.02 ± 5.20	46.06 ± 2.86	54.73 ± 2.07
EHDP + 2 h	—	—	49.30 ± 2.42	—

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

TABLE V

RATIO OF BONE: BLOOD ACTIVITY

	1 hour	2 hours	3 hours	4 hours
Control	9.54 ± 0.84	15.25 ± 1.68	21.21 ± 1.48	38.89 ± 2.36
EHDP −2 h	3.27 ± 0.27***	7.57 ± 0.78**	10.71 ± 1.27***	—
EHDP −1 h	3.42 ± 0.24***	8.84 ± 0.86**	15.34 ± 2.89*	—
EHDP with MDP	4.11 ± 0.17***	7.20 ± 0.39***	14.78 ± 1.35**	16.05 ± 0.99***
EHDP +1 h	—	6.61 ± 0.70***	16.13 ± 1.69*	19.67 ± 1.40***
EHDP +2 h	—	—	19.91 ± 3.19	—

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

TABLE VI

DOSE DEPENDENCY EXPERIMENT

	Bone %/g	Kidney %/g	Bladder % dose	Blood %/g	Blood: bone ratio
Control	1.83 ± 0.09	6.35 ± 0.79	20.72 ± 6.50	0.20 ± 0.06	9.54 ± 0.84
5 mg/kg	1.42 ± 0.06*	1.72 ± 0.25***	51.45 ± 1.25**	0.20 ± 0.01	7.37 ± 0.56
10 mg/kg	1.50 ± 0.11	8.39 ± 2.33	27.26 ± 6.72	0.27 ± 0.02	5.59 ± 0.44**
20 mg/kg	1.43 ± 0.08*	12.63 ± 2.00*	13.42 ± 8.26	0.32 ± 0.05*	4.49 ± 0.18***

Mean ± 1 SE. Significantly different from control level * <0.05, ** <0.01, *** <0.001.

levels of $^{99}Tc^{m}$, as indicated by bladder activity, were shown to correlate with the decreasing kidney activity ($p < 0.01$), and bladder volume correlated with contained activity ($p < 0.01$). Muscle levels at one hour were 0.36 ± 0.005, at two hours 0.017 ± 0.002, at three hours 0.007 ± 0.001 and at four hours 0.01 ± 0.002. These tissue levels correlated strongly with blood levels ($p < 0.001$).

Study groups

Bone activity. Overall EHDP significantly depressed bone activity, maximally if given early (−2 EHDP). The suppression was most marked at the one hour and three hour stages (Fig. 1). There was, however, a significant increase in bone activity in the two groups studied at four hours when compared with the control population. The recorded decrease

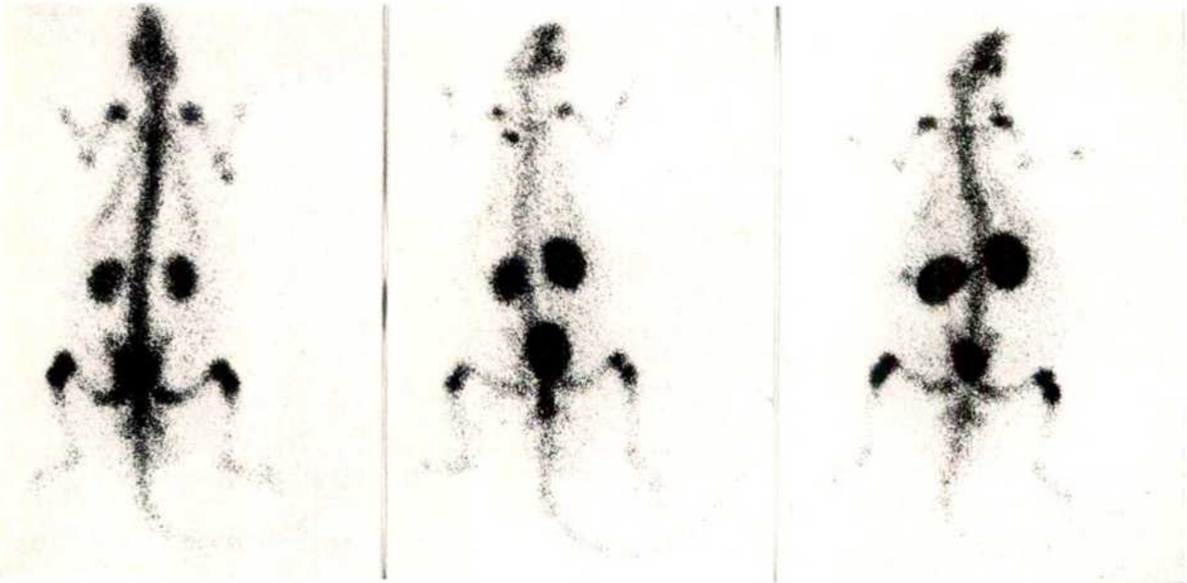


FIG. 1.

Scintigrams 3 h after administration of Tc-MDP, 300 000 events being recorded in each. (A) control, (B) −2 EHDP, (C) 0 EHDP.

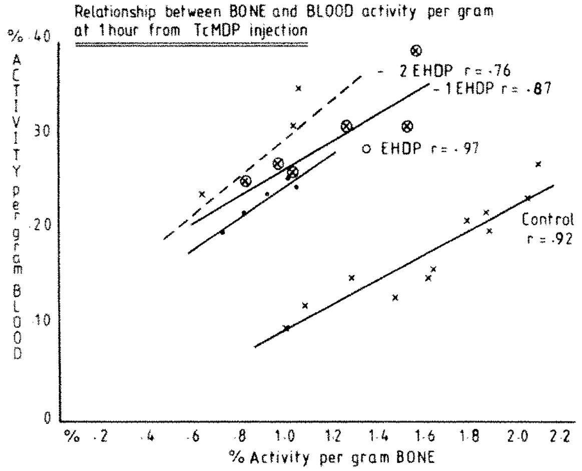


FIG. 2.

The relationship between bone and blood activity per gram 1 h after Tc-MDP injection is shown in four groups of animals—control (×), concurrent administration of EHDP and Tc-MDP (●), pre-injection by 1 h with EHDP (⊗) and pre-injection by 2 h with EHDP (dashed line and ×). Significant relationships are obtained in all groups except the last, in which a parallel trend is observed.

in activity was shown not to be dose-dependent (Table VI).

Renal activity. Renal activity was markedly affected in most of the study groups with significant increases being recorded. The effect was least marked in those groups where EHDP had been administered after Tc-MDP. Increased renal activity correlated with renal size ($r=0.46$, $p<0.05$). The alteration in renal activity, when compared with controls, was shown to be strongly dose-dependent ($r=0.76$, $p<0.001$). Renal activity was shown to be below normal with small doses of EHDP and increased with higher doses. The increased activity was associated again with an increase in renal size ($r=0.62$, $p<0.02$).

Bladder activity. There was a wide range of bladder activity in some groups. Significant reductions in bladder activity occurred in association with elevation of renal activity. This too was shown to be dose dependent ($r=0.98$, $p<0.001$).

Blood activity. Blood levels tended to be significantly elevated throughout the experimental groups although this effect was least marked at the three hour stage (Table III). The elevation of blood levels was also dose-dependent ($r=0.82$, $p<0.001$) and correlated strongly with an increasing renal activity ($r=0.85$, $p<0.001$). The combination of altered bone and blood activities throughout the study groups indicated highly significant changes from the control animals when expressed in terms of bone to blood activity ratio (Table V). The ratio demonstrates highly significant reduction in almost all study groups compared with the control population. Suppression of bone to blood ratios occurred even in the four-hour groups when elevation in absolute bone levels had been obtained. The bone to blood ratio was also demonstrated to be dose-dependent ($r=0.85$, $p<0.001$). There was no correlation between overall blood levels and bone levels in the study groups similar to the finding in the control population. However, significant correlation could be obtained between bone and blood activity at one hour from Tc-MDP injection in the 0 EHDP ($r=0.97$) and -1 EHDP ($r=0.87$). A non-significant trend was observed also in the -2 EHDP group ($r=0.76$) (Fig. 2).

DISCUSSION

The study reveals that the administration of unlabelled EHDP at or around the time of injection of Tc-MDP causes profound alterations in the distribution of the latter.

The extraction of Tc-MDP by bone in the control animals is shown to have peaked at one hour from injection and to correlate positively with the blood level at this stage. Bone activity thereafter declines but an increasing bone to background ratio is achieved by a progressive diminution in blood level secondary to renal excretion. The effect of loading with EHDP would appear to be an all-or-nothing phenomenon within the dose range examined in this study. There is universal suppression of bone activity despite higher blood levels and the maintenance of an overall correlation between the two at one hour. The mechanism of this suppression is unclear. It is known that low doses of EHDP suppress mineralization rates but have no effect on the overall balance between bone deposition and bone resorption in experimental animals, and that higher doses inhibit mineralization rates disproportionately, resulting in a net negative balance (Russell *et al.*, 1973). The time scale of this inhibition is not known. Bone accumulation of Tc-MDP is dependent upon blood supply and perfusion. Diphosphonates leave the capillary bed and diffuse across bone fluid to bind on hydroxyapatite (Hughes *et al.*, 1978). Since there is no indication that diphosphonates alter blood flow it must be assumed that the alterations in bone uptake observed in the present study reflect changes at the site of hydroxyapatite crystal deposition. There are no data available to indicate why increased deposition of Tc-MDP should have been observed in the four hour group. The implications for clinical skeletal scintigraphy from the results of this study may be considerable. If the suppression of bone activity following acute intravenous administration of EHDP were to occur also with chronic oral administration, in the management of disease such as Paget's, the interpretation of scintigraphy in the follow-up of patients must be open to question, particularly if pathological bone is similarly affected.

Although, clearly, the effects of EHDP on the skeleton are of prime importance, the renal effects may also be clinically significant. The addition of an EHDP load not only suppresses the renal excretion but causes an increased renal size, probably by inhibiting the excretion pathway (Tröhler *et al.*, 1973). The increased size and activity in the kidneys following EHDP in a dose-dependent fashion supports the concept of a relationship with solute load. It has also been implied that the excretion pathway can be blocked by oncolytic agents resulting in an increased renal activity (Lutrin *et al.*, 1978). There are no data available to indicate where in the kidneys the increased activity is situated. Most probably, since the urine volume was reduced in the present series, it is likely that it is proximal to the collecting system. However, the abnormal renal accumulation of Tc-MDP resulting from concurrent EHDP loading may have two important sequelae. Firstly, by inhibiting excretion and thereby causing high blood levels, a poor quality image is achieved, as judged by a bone/blood ratio. This may again give a false impression of resolution of disease. Secondly, persisting and elevated levels of Tc-MDP will result in an increased burden of renal radiation.

The alterations observed in the overall distribution of Tc-MDP caused by EHDP, though apparently deleterious, may have some clinical benefit. Lesions with a rich vascularity may be more obvious, particularly at the perfusion phase, by virtue of the increased blood-pool activity. Similarly, extra-osseous lesions may be more readily visualized by the relative suppression of bone activity, as has been previously reported in scanning myocardial infarction using Vitamin D_3 (Carr *et al.*, 1978). However, the toxic effects of intravenous EHDP observed in the present study, probably due to peptization with a fall in free calcium (Fleisch *et al.*, 1970), preclude its use in humans, and oral administration, not associated with severe side effect, is unsatisfactory because of very variable individual absorption rates (Michael *et al.*, 1972).

Acknowledgments

The authors express their gratitude for financial support by the Special Trustees of the Bristol Health District (Teaching); to Dr. E. Rhys Davies for guidance in the preparation of the manuscript and to Mrs. Jean French for secretarial expertise.

REFERENCES

Carr, E. A. Jr., Carroll, Mary and Montes, M., 1978. The use of adjunctive drugs to alter uptake of ^{99m}Tc-Sn-pyrophosphate by myocardial lesions and bone. *Life Sciences, 22*, 1261–74.

Fleisch, H., Bisaz, S., Care, A. D., Mühlbauer, R. C. and Russell, R. G. G., 1970. In *Calcitonin 1969*. (Heinemann, London), pp. 409–417.

Francis, M. D., 1969. The inhibition of calcium hydroxyapatite crystal growth by polyphosphonates and polyphosphates. *Calcified Tissue Research, 3*, 151–162.

Francis, M. D., Russell, R. G. G. and Fleisch, H., 1969. Diphosphonates inhibit formation of calcium crystals in vitro and pathological calcification in vitro. *Science, 165*, 1264–1266.

Hentzer, B., Jacobsen, H. H. and Asboe-Hansen, G., 1978. Fibrodysplasia (myositis) ossificans progressiva treated with disodium etidronate. *Clinical Radiology, 29*, 69–75.

Hughes, S., Khan, R. and Davies, R., 1978. The uptake by the canine tibia of the bone-scanning agent ^{99m}Tc-MDP before and after an osteotomy. *Journal of Bone and Joint Surgery, 60B*, 579–582.

Lentle, B. C., Russell, A. S., Heslip, P. G. and Percy, J. S., 1976. The scintigraphic findings in Paget's disease of the bone. *Clinical Radiology, 27*, 129–135.

Lutrin, C. L., McDougall, I. R. and Goris, M. L., 1978. Intense concentration of technetium 99m pyrophosphate in the kidneys of children treated with chemotherapeutic drugs for malignant disease. *Radiology, 128*, 165–167.

Meunier, P. J., Alexandre, C., Edouard, C., Mathieu, L., Chapuy, M. C., Bressot, C., Vignon, E. and Trechsel, U., 1979. Effects of disodium dichloromethylene diphosphonate on Paget's disease of bone. *Lancet*, i, 489–492.

Michael, W. R., King, W. R. and Wakim, J. M., 1972. Metabolism of disodium ethane-I-hydroxy-I-diphosphonate (disodium etidronate) in the rat, rabbit, dog and monkey. *Toxicology and Applied Pharmacology, 21*, 503–515.

Miller, S. W., Castronovo, F. P., Jr., Pendergrass, H. P. and Potsaid, M. S., 1974. Technetium-99m labelled diphosphonate bone scanning in Paget's disease. *American Journal of Roentgenology, 121*, 177–183.

Murphy, W. A., Whyte, M. P. and Haddad, J. G., 1980. Healing of lytic Paget's disease with diphosphonate therapy. *Radiology, 134*, 635–637.

Russell, R. G. G. and Fleisch, H., 1976. Pyrophosphate and diphosphonates. In *The Biochemistry and Physiology of Bone*. 2nd Ed. (Academic Press, New York), pp. 61–104.

Russell, R. G. G., Kislig, Anne-Marie, Casey, P. A., Fleisch, H., Thornton, J., Schenk, R. and Williams, D. A., 1973. Effect of diphosphonates and calcitonin on the chemistry and quantitative histology of rat bone. *Calcified Tissue Research, 11*, 179–195.

Smith, R., Russell, R. G. G. and Bishop, M., 1971. Diphosphonates and Paget's disease of bone. *Lancet, i*, 945–947.

Suziki, Y., Hisada, K. and Takeda, M., 1974. Demonstration of myositis ossificans by ^{99m}Tc pyrophosphate bone scanning. *Radiology, 111*, 663–664.

Tröhler, U., Treloar, M., Bonjour, J-P. and Fleisch, H., 1973. Net renal secretion of diphosphonates in rats: inhibition by phosphate. *European Journal of Clinical Investigation, 3*, 272.

1981, *British Journal of Radiology*, 54, 597–601

Cell labelling and cell damage with indium-111 acetylacetone—an alternative to indium 111 oxine

By Heather J. Danpure, Ph.D. and Safiye Osman, B.Sc.

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

(Received November 1980 and in revised form January 1981)

Abstract

The labelling of HeLa S3 cells with ^{111}In acetylacetone (^{111}In-acac) was studied together with cell damage, measured by the reduction in colony-forming ability of labelled cells. Using 2×10^5 cells/ml in Hepes saline buffer at pH 7.6 incubated with 7.4–185 kBq (0.2–5.0 μCi)/ml ^{111}In-acac, containing 0.19% acetylacetone for 15 minutes at room temperature, 60–80% ^{111}In was bound to the cells. The cell binding was linear with activity and resulted in an exponential reduction in colony forming ability and a D_0 of 26 kBq (0.7 μCi)/2×10^5 cells. Radiation was shown to be the major cause of cell damage. It is concluded that ^{111}In-acac is preferable to ^{111}In oxine because it is soluble in physiological buffers, which eliminates the use of ethanol; it is quick and easy to prepare; and compared with previous results using HeLa S3 cells labelled with ^{111}In oxine, ^{111}In-acac gives much more reproducible results and is no more toxic. Clinically, ^{111}In-acac was shown to give similar results to ^{111}In oxine.

The metal chelate ^{111}In acetylacetone (^{111}In-acac) was originally prepared by Sinn *et al.* (1974) as a compound to label erythrocytes, but was subsequently developed by Sinn and Silvester (1979) as an alternative to ^{111}In oxine for labelling leukocytes as it is quicker and easier to prepare.

In this paper the labelling of HeLa S3 cells with ^{111}In-acac and the resulting cell damage, assayed by measuring the colony-forming ability of labelled cells, is described and compared with previously reported cell damage caused by labelling cells with ^{111}In oxine. From the results it is concluded that ^{111}In-acac has certain advantages over ^{111}In oxine and can be used as an alternative to ^{111}In oxine for labelling cells for clinical and biological use.

Materials and Methods

Cell culture

Cultures of HeLa S3 cells were routinely maintained in Eagle's minimum essential medium containing streptomycin, penicillin, 20 mM Hepes buffer and 15% fetal calf serum (ME-15). For experiments, one-day old cultures were trypsinized and the cells washed twice in 20 mM Hepes 0.8% saline buffer at pH 7.6, and resuspended in the same buffer at twice the required cell concentration.

Acetylacetone solutions

All solutions of acetylacetone were made at double strength to allow for dilution with equal volumes of cells in Hepes–saline buffer at pH 7.6. Stock solutions of Hepes-buffered acetylacetone containing 0.38% v/v acetylacetone (Sigma), 20 mM Hepes (acid form), 0.8% w/v NaCl in water for injection were adjusted to pH 7.6 with 1M NaOH. For stock solutions containing more than 0.38% v/v acetylacetone the amount of NaCl was reduced to give a final osmolality of 290–310 mOsmoles when diluted with equal volumes of Hepes–saline buffer at pH 7.6 (290–300 mOsmoles). All the solutions were filter-sterilized and stored at 4°C in the dark.

Cell labelling (standard procedure)

Two-and-a-half millilitre aliquots of washed cells at 4×10^5/ml in Hepes–saline buffer were added to 2.5 ml ^{111}In-acac previously made by adding 50 μl $^{111}InCl_3$ (kindly supplied by the Radiochemical Centre and diluted in 0.04M HCl to the required concentration) to 2.5 ml 0.38% v/v acetylacetone in 20 mM Hepes–saline buffer and incubated for 15 minutes at room temperature (20–25°C). It was also possible to achieve good labelling by resuspending cells in 5 ml Hepes–saline containing 0.19% acetylacetone followed by addition of $^{111}InCl_3$ and incubation at room temperature for 15 minutes. Cell labelling was stopped by addition of 5 ml tissue culture medium containing 30% serum (ME-30) and samples were removed to determine the initial cell binding, while the remaining cells were washed twice with 10 ml ME-15. The cell number was determined using a haemocytometer and cell-bound radioactivity was measured on a Wallac Ultragamma Spectrometer.

To study the effect of temperature, incubation time, cell number and acetylacetone concentration on the binding of ^{111}In-acac to HeLa S3 cells, the appropriate modifications to the standard procedure were made using 185 kBq (5 μCi)/ml complex throughout.

Cell damage

The damage produced by labelling HeLa S3 cells with ^{111}In-acac was assayed by measuring their ability to divide and form visible colonies containing 50 or more cells. Cells were labelled at 2×10^5/ml in buffer under standard conditions, *i.e.* with ^{111}In-acac containing 0.19% acetylacetone and 7.4–185 kBq (0.2–5.0 μCi)/ml ^{111}In for 15 minutes at room temperature. The labelled cells were washed and replicate samples of 200 cells were plated into petri dishes containing 7 ml ME-15 and incubated for colony formation as previously described (Danpure and Tyrrell, 1976). Cells treated with 0.19% acetylacetone in buffer were used as controls. For each dose of ^{111}In the amount of radioactivity bound per 2×10^5 cells was determined before and after washing. Unless otherwise stated, all the results are for washed cell samples.

To determine the effect of the radiation from the decay of ^{111}In on the colony-forming ability of HeLa S3 cells, the same batches of $^{111}InCl_3$ that were used to measure cell damage were left to decay and then used to prepare fresh solutions of "indium-acac". Cells were then treated with an amount of the decayed preparation equivalent to the maximum concentration previously used and their colony-forming ability measured.

The toxicity of acetylacetone was determined by measuring the colony-forming ability of HeLa S3 cells treated with varying concentrations of acetylacetone (0.19–1.9% v/v) under standard conditions of time and temperature, followed by washing and plating as previously described.

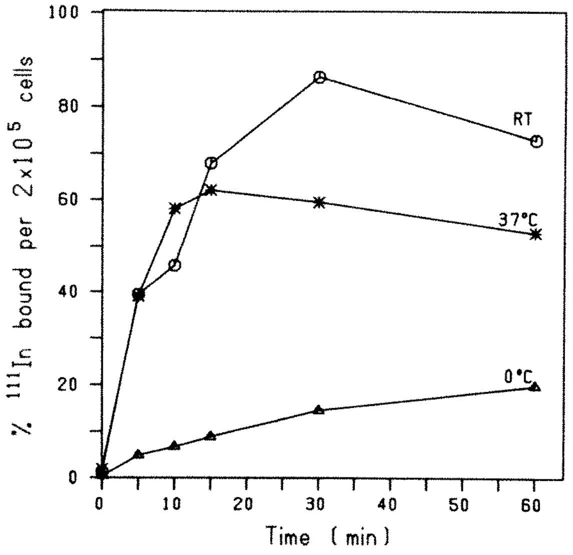


FIG. 1.

The effect of incubation time and temperature on the binding of ^{111}In-acac to HeLa S3 cells. RT indicates incubation at room temperature (20–25°C).

RESULTS

Cell-labelling

An example of the effect of incubation time and temperature on the percentage of ^{111}In bound to washed HeLa S3 cells labelled under standard conditions with 185 kBq (5 μCi)/ml complex is shown in Fig. 1. Incubation at room temperature (20–25°C) in this instance produced a higher uptake than incubation at 37°C, reaching a peak of 86% after 30 minutes. However, in a few experiments the uptake at 37°C was greater. In all experiments the percentage of ^{111}In bound to the cells reached a plateau after 15–30 minutes incubation at room temperature or 37°C.

The effect of cell concentration on the binding of ^{111}In-acac to HeLa 3S cells is shown in Table I. An increase from 1.5×10^5 to 10^7 cells/ml produced a twofold increase in percent ^{111}In bound to the cells but a 35 fold reduction in activity per cell. In this experiment an unusually large amount of the ^{111}In was lost from the cells during washing, but in all other experiments it was less than 10% irrespective of cell concentration. Where lower cell concentrations were used (2×10^3–10^5/ml), only 5–35% ^{111}In was initially bound to the cells (results not shown).

The concentration of acetylacetone association with the ^{111}In, most of which was not complexed to the ^{111}In, greatly affected the amount of ^{111}In bound to the cells. An optimum binding of 83% with 2×10^5 cells/ml was achieved with 0.19% acetylacetone, but at concentrations above and below these the percentage binding was reduced (Fig. 2).

HeLa S3 cells incubated with $^{111}InCl_3$ in buffer, or with ^{111}In-acac containing 0.19% acetylacetone in medium plus serum (ME-15), showed very low levels of cell binding (1–2%).

TABLE I

EFFECT OF CELL CONCENTRATION ON THE BINDING OF ^{111}IN-ACAC TO HeLa S3 CELLS

Cell concentration/ml $\times10^5$	Percent ^{111}In* bound to cells		μCi (37 kBq)/ 2×10^5 washed cells
	Initially†	After washing	
1.46	65	39	2.68
4.71	76	56	1.19
7.75	77	54	0.69
21.0	79	61	0.29
44.4	88	78	0.18
102.0	87	79	0.077

*All cells were incubated with 185 kBq (5 μCi)/ml ^{111}In-acac for 15 min at room temperature.

†Difference between ^{111}In in samples before and after removal of cells.

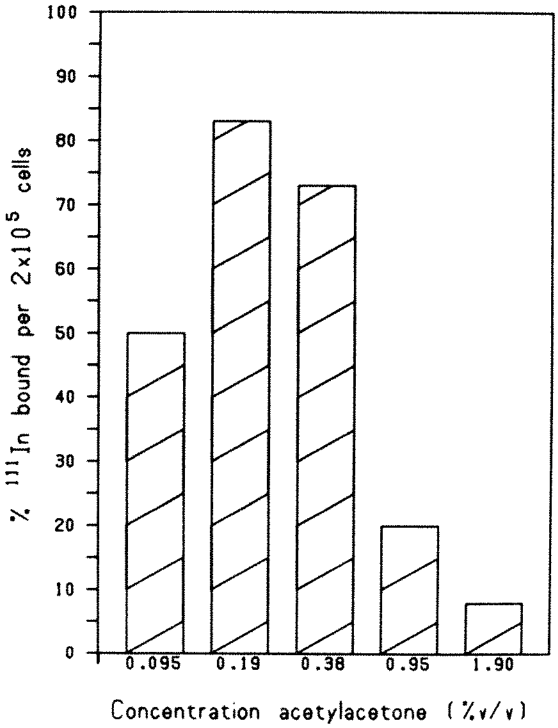


FIG. 2.

The effect of acetylacetone concentration on the binding of ^{111}In-acac to cells incubated for 15 minutes at room temperature.

Cell damage

Neither 0.19% acetylacetone nor up to 740 kBq/ml (20 μCi/ml) $^{111}InCl_3$ alone in Hepes-saline buffer reduced the colony-forming ability of HeLa S3 cells treated at 2×10^5 cells/ml for 15 minutes at room temperature. On the other hand cells treated under the same conditions with ^{111}In-acac containing 0.19% acetylacetone and 7.4–185 kBq/ml (0.2–5 μCi/ml) ^{111}In showed a linear increase in activity bound per 2×10^5 cells (Fig. 3A) and an exponential reduction in colony-forming ability (Fig. 3B). The experiments were repeated several times but for clarity only the results from one experiment are shown. The plating efficiency of control cells was 70–95% in all experiments. From Fig. 3B the dose to produce one lethal event, D_0, (equivalent to $1/e$ or 37% survival) was 26 kBq (0.7 μCi)/2×10^5 washed cells, which is equivalent to 2180 cGy (rad) per cell if all the ^{111}In decayed. This estimate of dose is based on a modification of the calculation of Silvester (1979) for HeLa S3 cells of approximately 16μm diameter (Steinkamp *et al.*, 1976).

However, when HeLa S3 cells were labelled with ^{111}In-acac at 2×10^6 cells/ml instead of 2×10^5/ml, the percent ^{111}In bound to the cells increased as in Table I but the lower binding per cell resulted in proportionately less effect on the colony-forming ability of the cells, demonstrating that cell damage is directly related to the amount of ^{111}In bound to the cell.

Similarly, when cells were labelled with ^{111}In-acac in tissue-culture medium containing serum (ME-15) rather than buffer, no reduction in colony forming ability was observed because the amount of ^{111}In bound to cells was only 1–2%. But if the activity was greater than 740 kBq/ml (20 μCi/ml!) the amount of binding was sufficient to reduce the colony-forming ability of the labelled cells.

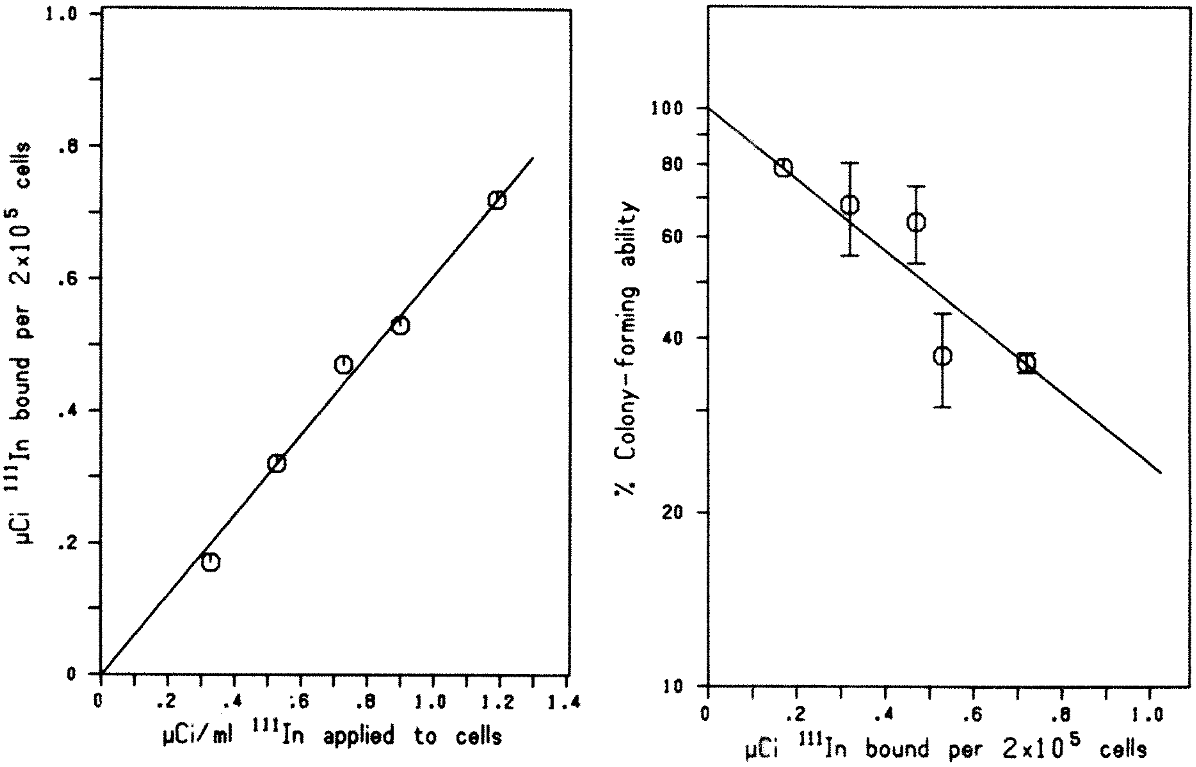
To ascertain the role of the radiation from ^{111}In in producing cell damage, HeLa cells were "labelled" with indium acetylacetone freshly prepared from the same batches of $^{111}InCl_3$ as used previously but after the ^{111}In had decayed. In these experiments no reduction in colony-forming ability was observed.

DISCUSSION

This paper confirms the previous observations (Sinn and Silvester, 1979) that ^{111}In-acac is an efficient cell-labelling agent with some similar properties to the widely-used metal chelate ^{111}In oxine (Thakur *et al.*, 1977; Goodwin, 1978). Both compounds are lipid-soluble metal complexes which rapidly and non-specifically bind to cells provided the cells are labelled in the absence of serum transferrin which dissociates the complex (Sarin and Munshi, 1977). For example, with 2×10^5/ml HeLa cells incubated with ^{111}In-acac in Hepes–saline buffer for 15 minutes at room temperature, approximately 70% ^{111}In was bound to the cells, whereas with cells suspended in Eagle's medium containing 15% fetal calf serum it was reduced to 1–2%.

The most important factor in achieving good cell labelling with ^{111}In-acac was the concentration of acetylacetone used to prepare the ^{111}In-acac complex. Using 2×10^5/ml HeLa cells a complex containing 0.19% acetylacetone gave maximum cell binding with higher and lower concentrations showing a reduction (Fig. 2). However, if the cell concentration was doubled to 4×10^5/ml the maximum binding was not reduced until the acetylacetone concentration exceeded 0.95%. But as acetylacetone alone was toxic above 0.38% at both cell concentrations, it would not be advisable to increase the acetylacetone concentration above that required to give good cell labelling.

Comparison of the cell labelling properties of ^{111}In-acac with ^{111}In oxine, using HeLa S3 cells at 2×10^5/ml in a serum-free medium, showed that with



A FIG. 3. B

(A) The amount of ^{111}In bound per 2×10^5 washed HeLa S3 cells in relation to the amount of ^{111}In-acac applied to the cells using the standard labelling and washing procedure.

(B) The reduction in colony-forming ability of HeLa S3 cells produced by the levels of ^{111}In binding from ^{111}In-acac shown in Fig. 3A.

^{111}In-acac high levels of cell binding (approximately 70%) were achieved with low cell numbers (2×10^5/ml), that ^{111}In binding was linear with activity over the range 3.7–740 kBq (0.1–20 µCi), and that ^{111}In-acac made from different batches of $^{111}InCl_3$ gave similar levels of cell binding. This contrasted with previous results using HeLa S3 cells labelled with ^{111}In oxine (Danpure *et al.*, 1979; Chisholm *et al.*, 1979) where the levels of ^{111}In cell binding were generally lower and variable (2–60%) and non-linear with activity and where the amount of binding changed with every batch of $^{111}InCl_3$ used to make the ^{111}In oxine.

Similar comparison between cell damage to HeLa S3 cells produced by ^{111}In-acac and ^{111}In oxine is more difficult as the ^{111}In oxine data were so variable (Danpure *et al.*, 1979; Chisholm *et al.*, 1979). Attempts to obtain improved results with ^{111}In oxine by washing the HeLa S3 cells after labelling were unsuccessful. The available data suggest that the levels of cell damage produced by the two complexes may be similar. The ^{111}In-acac survival data from several experiments all fit the line shown in Fig. 3B and give a D_0 of 26 kBq (0.7 µCi)/2×10^5 cells which is equivalent to an initial binding of 4×10^4 indium atoms per cell. This amounts to a dose of 2180 cGy (rad)/cell after decay of all the indium. However, the dose received by the cells within the first few days after labelling is likely to determine their ability to divide, and this dose would be much lower. Hofer *et al.* (1975) have used the same technique with L1210 cells and have measured the cell damage from two other γ-emitting internally deposited radionuclides ^{124}I and ^{67}Ga, which like ^{111}In decay by electron capture releasing a number of Auger electrons. With ^{67}Ga citrate labelled cells they obtained a shoulder on their survival curve indicating that the cells could tolerate low doses of ^{67}Ga without loss of viability, whereas the apparent exponential survival of HeLa S3 cells labelled with

^{111}In-acac would indicate no tolerance to low doses of ^{111}In. Hofer further showed that it was the proportion of radiation reaching the cell nucleus which was responsible for the cell damage. Similar information about the location of ^{111}In within the HeLa cell is not yet available.

A comparison of the tissue distribution of rat thoracic-duct lymphocytes labelled with ^{111}In-acac containing 0.19% acetylacetone, with those labelled with ^{111}In oxine, showed that with more than 185 kBq (5 μCi) of either ^{111}In complex/10^8 cells the cells failed to localize in the lymph nodes, indicating that the labelled cells were damaged (P. M. Chisholm, personal communication).

Both the ^{111}In oxine and ^{111}In-acac data with HeLa S3 cells indicate that radiation from the decay of ^{111}In is the major cause of cell damage as cells treated with non-radioactive preparations showed no reduction in colony-forming ability. The same conclusion was reached when rat thoracic duct lymphocytes were labelled with ^{111}In-acac (P. M. Chisholm, personal communication).

For clinical and biological use, ^{111}In-acac has several advantages over ^{111}In oxine and is recommended by the authors as preferable to ^{111}In oxine. First, ^{111}In-acac can be very rapidly and easily prepared just before use by the addition of $^{111}InCl_3$ in acid to sterile solutions of 0.38% acetylacetone in Hepes–saline buffer to which an equal volume of cells in buffer is subsequently added. The solution of acetylacetone in Hepes–saline buffer can be stored in the dark at 4°C for several months without affecting its ability to label cells. This avoids the chloroform extraction which is necessary with ^{111}In oxine (Thakur *et al.*, 1977). Second, ^{111}In-acac is administered to cells in physiological buffer which avoids the necessity for addition of ethanol to cells as used with ^{111}In oxine. This is important as ethanol is known to damage cells (Freund and Forbes, 1976) and could not be used with HeLa S3 cells at concentrations in excess of 1% without reducing their colony-forming ability. Commercial preparations of ^{111}In oxine in physiological solutions are now also available, but were not tested here. Finally, with HeLa S3 cells, ^{111}In-acac is no more toxic than ^{111}In oxine, gives much more reproducible cell labelling and cell damage than ^{111}In oxine, and is not affected by any variation in the composition of different batches of $^{111}InCl_3$.

^{111}In-acac has also been shown to be satisfactory for clinical use and white blood cells, red blood cells and platelets are now being labelled with ^{111}In-acac at Hammersmith Hospital and are giving similar results in patients to ^{111}In oxine (A. M. Peters, personal communication).

REFERENCES

Chisholm, P. M., Danpure, H. J., Healey, G. and Osman, S., 1979. Cell damage resulting from the labelling of rat lymphocytes and HeLa S3 cells with In-111 oxine. *Journal of Nuclear Medicine, 20,* 1308–1311.

Danpure, H. J., Osman, S. and Hesslewood, I., 1979. Cell damage associated with ^{111}In-oxine labelling of a human tumour cell line (HeLa S3). *Journal of Labelled Compounds and Radiopharmaceuticals, 16,* 116–118.

Danpure, H. J. and Tyrrell, R. M., 1976. Oxygen-dependence of near UV (365 nm) lethality and the interaction of near UV and X-rays in two mammalian cell lines. *Photochemistry and Photobiology, 23,* 171–177.

Freund, G. and Forbes, J. T., 1976. Alcohol toxicity in cell culture. *Life Sciences, 19,* 1067–1072.

Goodwin, D. A., 1978. Cell labelling with oxine chelates of radioactive metal ions. Techniques and clinical implication. *Journal of Nuclear Medicine, 19,* 557–559.

Hofer, K. G., Harris, C. R. and Smith, J. M., 1975. Radio-toxicity of intracellular ^{67}Ga, ^{125}I and ^{3}H. Nuclear and cytoplasmic radiation effects in murine L1210 leukaemia. *International Journal of Radiation Biology, 28,* 225–241.

Sarin, R. and Munchi, K. N. I., 1977. Stepwise stability constants and thermodynamic functions of In(111) complexes with some substituted derivatives of quinoline and pyridine. *Indian Journal of Chemistry, 15A,* 327–329.

Silvester, D. J., 1979. Consequences of indium-111 decay *in vivo*. Calculated absorbed radiation dose to cells labelled by indium-111 oxine. *Journal of Labelled Compounds and Radiopharmaceuticals, 16,* 193.

Sinn, H., Georgi, P., Clorius, J. and Maier-Borst, W., 1974. Die Markierung von Erythrozyten mit radioaktiven Indiumisotope. *Nuklear Medizin* (Stuttgart), *13,* 180–185.

Sinn, H. and Silvester, D. J., 1979. Simplified cell labelling with Indium-111 acetylacetone. *British Journal of Radiology, 52,* 758–759.

Steinkamp, J. A., Hansen, K. M. and Crissman, H. A., 1976. Flow microfluorimetric and light scattering measurement of nuclear and cytoplasmic size in mammalian cells. *Journal of Histochemistry and Cytochemistry, 24,* 292–297.

Thakur, M. L., Lavender, J. P., Arnot, R. N., Silvester, D. J. and Segal, A. W., 1977. Indium-111 labelled autologous leukocytes in man. *Journal of Nuclear Medicine, 18,* 1012–1019.

1981, *British Journal of Radiology*, *54*, 602–605

Induction of spinal cord paralysis by negative pi-mesons

By H. I. Amols, Ph.D. and J. M. Yuhas, Ph.D.

University of New Mexico Cancer Research and Treatment Center, Albuquerque, New Mexico 87131, USA

(*Received August 1980 and in revised form December 1980*)

ABSTRACT

As part of our investigations on late non-neoplastic injury induced by negative pi-mesons (pions), a series of studies have been performed using pion beams for the induction of spinal cord paralysis in the Fisher 344 rat. Groups of rats were exposed to 1, 5 or 15 daily doses of peak pions or X rays. Paralysis appeared earlier after treatment with pions than after X rays even in a comparison of groups with similar final incidences.

A single dose RBE for spinal cord paralysis of 1.3 was found. The RBE rises to a value of 3.2 if the total dose is given as a series of 15 daily exposures. These RBEs are far larger than we have observed using other late injury end-points, such as tubular degeneration in the kidney or fibrosis and sclerosis in the support structures of the colon for which the single dose RBE is less than 1.2.

The biological and/or physical basis for the high sensitivity of the spinal cord to peak pions has not yet been resolved, but these data have suggested caution in exposing the spinal cord to peak pions in our clinical trials.

Phase II and Phase III clinical trials of negative pi-mesons (pions) are now in progress at the Los Alamos Meson Facility (LAMPF) (Kligerman *et al.*, 1979). As part of this project, an ongoing study of late, non-neoplastic injury induced by pion beams on various critical organs and tissues has been undertaken. Previous communications have reported results for pion-induced injury to the mouse foot and skin (Raju and Carpenter, 1978; Yuhas *et al.*, 1979), mouse testis (Gomez *et al.*, 1977), mouse kidney (Jordan *et al.*, 1979), and the rat colon (Yuhas *et al.*, 1979). In this note, we present results for the induction of spinal-cord paralysis in Fisher 344 rats.

These studies were deemed necessary owing to the importance of spinal-cord injury in radiotherapy. Exposure to radiation of the spinal cord is often of critical importance in treatment planning, especially for cancers of the head and neck. Tumours in this area are currently being scheduled for pion radiotherapy. Early studies of spinal-cord injury (Yuhas *et al.*, 1979) were limited owing to the extremely low dose-rates available at that time. These preliminary results, however, indicated that the single dose RBE for spinal-cord paralysis could be as high as 1.5. This is significantly higher than for other normal tissues studied. Consequently, when higher pion dose-rates became available, studies of spinal-cord injury were reinitiated.

METHODS AND PROCEDURES

Three-month-old Fisher 344 female rats were used in these investigations. For all animals, a 2 cm segment of the lumbar spine (L1–L4) was irradiated with either negative pions or X rays. The animals were observed weekly through the first year post-irradiation for evidence of paralysis. No grading scale was used other than the simple criterion of paralysis or no paralysis.

X-ray exposures were made with a sharply collimated (2 × 2 cm^2) beam of 300 kV X rays, 2 mm Cu HVL, at a dose-rate of approximately 80 cGy (rad) per minute. The animals were anaesthetized before exposure and positioned in a Lucite immobilization cast. Pion exposures were made using a nearly identical procedure, also at 80 cGy/min.

For the pion exposures, however, special procedures had to be undertaken in order to insure that: (1) the lumbar spine was uniformally irradiated; and (2) the pion dose to the gut was minimized.

The technique used to accomplish this is shown schematically in Fig. 1. A 2 × 3 cm^2 Cerrobend collimator was fabricated, the edge of which is shown as a dark line on Fig. 1. The rats were positioned asymetrically under the collimator, so that the dose gradient between the lumbar spine (hatched area of Fig. 1) and the gut was maximized.

In this way, the dose to the gut was kept below 30–50% of the dose to the spinal cord. All pion exposures were done at the dose maximum position using a narrow peak, as shown in the upper left hand corner of Fig. 1. Before exposure, all animals were aligned relative to the collimator opening using a fluoroscopic unit to assure proper set up. Dose-rates for both pions and X rays were measured by use of small capsules of TLD powder.

RESULTS

At least five animals were used at each dose. The treatment regimes tested comprised single doses, five fractions in five days and 15 fractions in 18 days. The schedule for the 15 fraction experiment was constrained by the accelerator schedule which was five days on, two days off, four on, one off and six on. Animals were observed weekly for signs of paralysis, up to one year post-irradiation. After one year, the total number of paralysed animals in each group was noted. The results are shown in Fig. 2 which plots

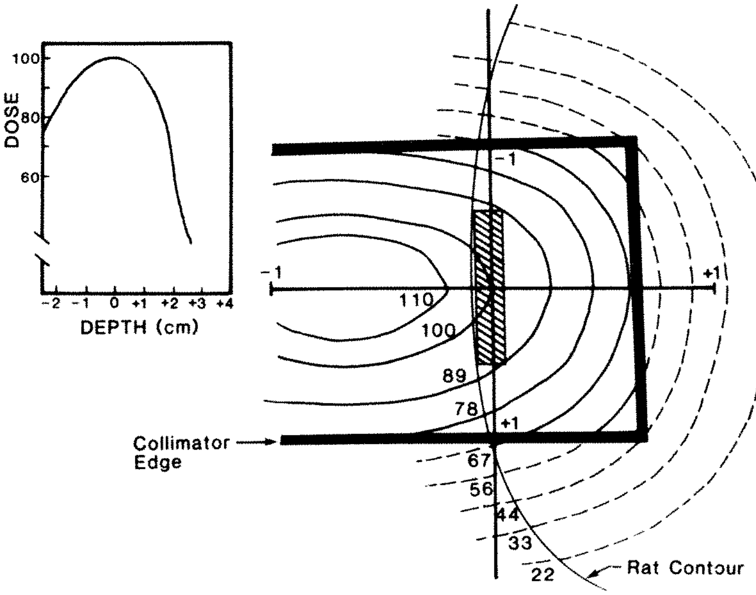


FIG. 1.

Dose distributions for pion irradiation of the spinal cord. The edge of the collimator is indicated by the dark contour. The treatment region is indicated by the hatched area. The animals were immobilized in a Lucite jig, the outline of which is denoted by the arc to the left of the treatment region. The inset in the upper left corner shows the depth-dose distribution. The centre of the treatment region was positioned at depth zero.

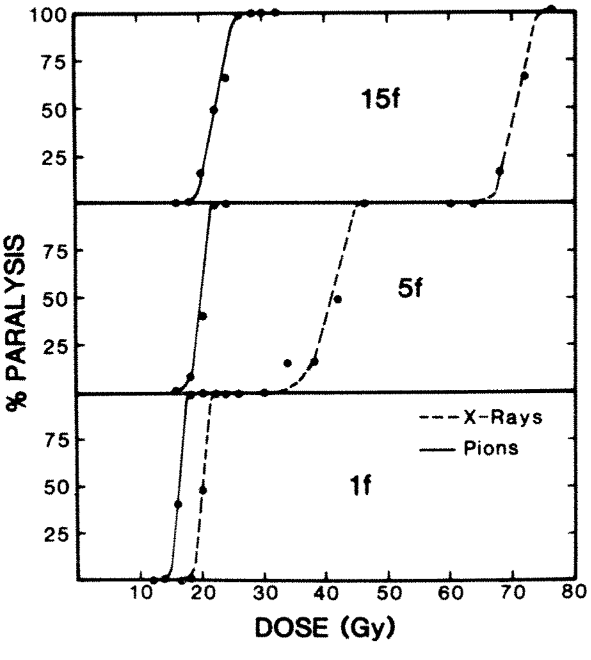


FIG. 2.

Percentage paralysis vs. total dose for pions (solid curves) and X rays (dashed curves), for 1, 5 and 15 fractions.

the percentage of animals paralysed vs. total dose, for pions and X rays given in one, five and 15 fractions.

The familiar sigmoid response curve is evident. In addition, the RBE for pions is seen to increase for fractionated treatments. Table I records the RBE values for the ED_{50} (*i.e.* the dose required for paralysis of 50% of the exposed animals). The RBE for a 15 fraction treatment is 3.2. The single-dose RBE of 1.3 also confirms that found in previous studies (Yuhas *et al.*, 1979). These RBEs are far larger than we have observed using other late-injury endpoints such as tubular degeneration in the kidney, or fibrosis and sclerosis in the support structures of the colon. As an example, in the latter two tissues, the single dose RBE is less than 1.2, and fractionated RBEs are less than 1.7.

TABLE I

DOSE AND RBE FOR 50% PARALYSIS

	X-ray dose	Pion dose	RBE
1 fraction	2083 ± 117	1604 ± 117	1.3
5 fractions	4176 ± 315	2012 ± 166	2.1
15 fractions	7103 ± 217	2236 ± 184	3.2

In addition to the unusually large RBE observed, the induction of spinal cord paralysis by negative pions appears to develop earlier than that caused by X rays. After exposure to pions, signs of paralysis became evident between three and four months after exposure. In the X-ray-treated animals, however, no paralysis was evident until at least five to six months after exposure. This difference remained valid even when groups with the same final incidences of paralysis were observed.

DISCUSSION AND CONCLUSIONS

The biological and/or physical basis for the high sensitivity of the spinal cord to peak pions has not yet been resolved, nor has the difference in temporal development of spinal-cord injury been explained. However, similar qualitative effects, on the induction of spinal-cord injury by 14 MeV neutrons, have been observed by van der Kogel (1979) who found that:

(1) paralysis after neutron irradiation occurs sooner than after X-irradiation; and

(2) the RBE for paralysis following neutron irradiation is higher than for other normal tissues.

Van der Kogel (1979) has also noted that the mechanisms of radiation damage appeared to be similar for neutrons and X rays. Both radiations produce lesions which are characterized by demyelination and necrosis of nerve roots. Although no histological studies were made on the pion-irradiated animals, one can assume that the lesions are also similar in nature.

In fact, as shown in Fig. 3, the data obtained from our pion experiments and those from van der Kogel's neutron experiments are remarkably similar. Plotted here are values of the ED_{50} vs. number of fractions for pions, neutrons and X rays. There is a slight difference in the absolute sensitivity of our animals compared with van der Kogel's (who used three-month-old male, WAG/Rij rats), but the RBEs are very nearly identical. This is seen more clearly in Fig. 4 in which RBE is plotted against fraction size for both sets of data. The rapid increase in RBE as fraction size is decreased is also clearly evident.

While an increase in RBE with decreasing fraction size is a well-known phenomenon, the magnitude of the increase for spinal cord appears to be far larger than for other normal tissues irradiated by pions, such as skin, kidney and colon (Yuhas *et al.*, 1979).

The similarity in RBE for pions and neutrons appears to be somewhat of an anomaly, as most tissues studied previously seem to indicate that pions have a lower biological effectiveness than do neutrons for both single and multifraction regimes. An excellent review of these data has been made by Raju (1980). Lower pion RBEs would also be expected from physical arguments.

Microdosimetric measurements on a pion beam very similar to the one used in these studies indicate that the dose-mean lineal energy varies across the peak region from 38–57 keV/μm (Amols *et al.*, 1976). Therapeutic neutron beams on the other hand have dose-mean lineal energies of 60–100 keV/μm (Amols *et al.*, 1977; Rodgers and Gross, 1974). Thus pions have a lower mean LET than do neutrons.

It appears then that the mechanisms involved in producing spinal cord paralysis are unusually

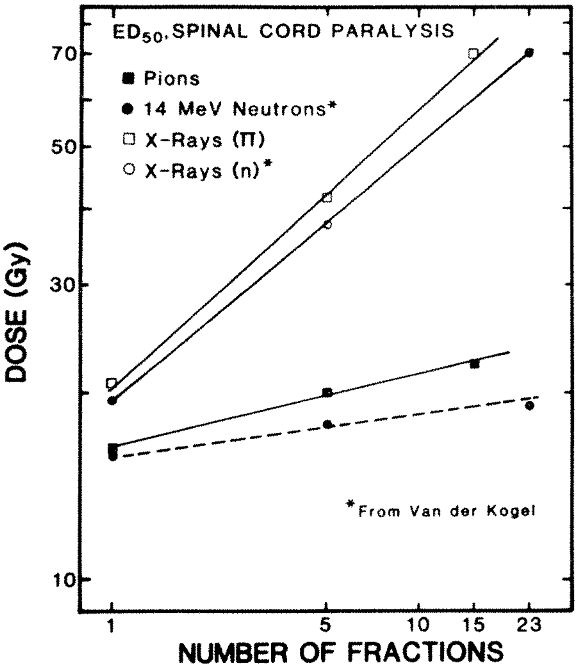


FIG. 3.

ED_{50} vs. number of fractions for X rays, pions and neutrons (includes results from van der Kogel, 1979).

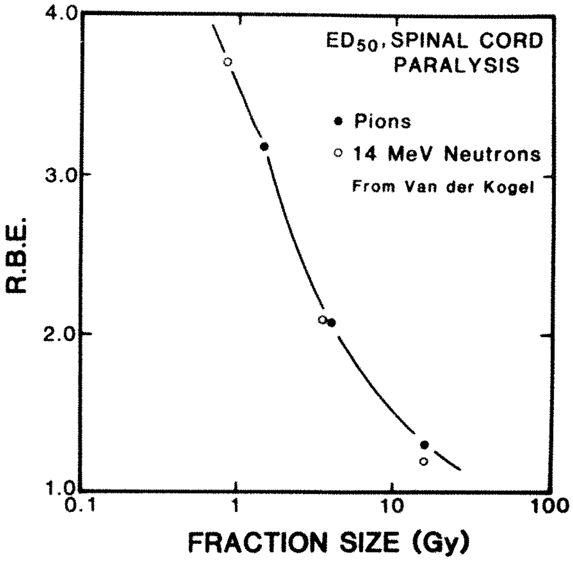


FIG. 4.

RBE vs. fraction size for pions (solid circles) and neutrons (open circles) (van der Kogel, 1979).

sensitive to pions. While this phenomenon is not clearly understood, these data do suggest that spinal cord dose may be a limiting factor in the irradiation of certain tumours with pions.

ACKNOWLEDGMENTS

These investigations were supported by USPHS Grant CA14052, NCI, Division of Research Resources and Centers. We would like to thank J. Butler for assistance with animal care and irradiations.

REFERENCES

AMOLS, H. I., DICELLO, J. F. and LANE, T., 1976. Microdosimetry of negative pions. In *Proceedings of the 5th Symposium on Microdosimetry*. Ed. J. Booz and H. Ebert, (Harwood Academic Pub., Commission of the European Communities, Brussels), pp. 911–928.

AMOLS, H. I., AWSCHALOM, M., COULSON, L., DICELLO, J., JOHNSON, S. and THEUS, R., 1977. Physical characterization of neutron beams produced by protons and neutrons of various energies bombarding beryllium and lithium targets of several thicknesses. *Medical Physics, 4*, 486–493.

GOMEZ, L. S., SMITH, D. M., DICELLO, J. F. and AMOLS, H. I., 1977. Effects of negative pions and X-rays on testes, weight loss and spermatogenic stem cell renewal in mice. *Radiation Research, 70*, 672.

JORDAN, S. W., YUHAS, J. M., KEY, C. R., HOGSTROM, K. H., BUTLER, J. L. and KLIGERMAN, M. M., 1979. Comparative late effects of X-rays and negative pi-mesons on the mouse kidney. *American Journal of Pathology, 97*, 315–326.

KLIGERMAN, M. M., VON ESSEN, C. F., KHAN, M. K., SMITH, A. R., STERNHAGEN, C. J. and SALA, J. M., 1979. Experience with pion radiotherapy. *Cancer, 43*, 1043–1051.

RAJU, M. R. and CARPENTER, S. G., 1978. A heavy particle comparative study. IV. Acute and late reactions. *British Journal of Radiology, 51*, 720–727.

RAJU, M. R., 1980. *Heavy Particle Radiotherapy*. (Academic Press, New York).

RODGERS, R. C. and GROSS, W., 1974. Microdosimetry of monoenergetic neutrons. In *4th Symposium on Microdosimetry*. Ed. J. Booz and H. Ebert, (Commission of the European Communities, Luxembourg), pp. 1027–1042.

VAN DER KOGEL, A. J., 1979. Late effects of radiation on the spinal cord (Ph.D. thesis). Radiobiological Institute of the Organization for Health Research TNO, Rijswijk, Netherlands.

YUHAS, J. M., LI, A. and KLIGERMAN, M. M., 1979. Present status of the proposed use of negative pi-mesons in radiotherapy. In *Advances in Radiation Biology, 8*, Ed. J. Lett. (Academic Press, New York), pp. 51–83.

Book review

Fast Neutrons in the Treatment of Cancer. By Mary Catterall and D. K. Bewley, pp. 388, 1979 (Academic Press, New York/London), £22·40.
ISBN 0–12–790820–X

This book is the best and most comprehensive account available of every aspect of fast neutron therapy, and is written by two outstanding members of an MRC unit that has now functioned virtually continuously for 25 years and is the most experienced unit of its kind in the world. The book falls naturally into two sections, each being the province of one of the two authors, but it does not give the impression of being two separate monographs coerced into the same covers, for the authors have produced a surprising degree of uniformity of style and presentation.

The first section of the book details the radiobiological and physical properties of fast neutrons that justify the continuing attempts to overcome the engineering and financial difficulties of producing a clinically adequate fast neutron source. The second section concerns itself with an account of how, and with what results, an enviably large number of patients with malignancies in a wide variety of sites has been treated: this account includes a detailed analysis of the prospective randomized trial (FN versus photons) in head and neck cancer. The clinical reporting occasionally adopts an anecdotal flavour, and more than once a hint of "special pleading" suggests itself. These trivial reservations apart, the clinical account concerns itself with the largest and most consistently treated series of fast neutron patients ever accumulated. Imperfections in the design of the prospective trial have led to now widely acknowledged doubts about the comparability of the two trial groups, and about the statistical validity of the trial's conclusion—namely, that fast neutrons are demonstrably superior to conventional treatment of primary and secondary malignancies at many sites. To date, most other fast neutron workers have reported less encouraging results than the Hammersmith group and some have reported conflicting results.

The haze surrounding the proper place of fast neutrons in radiotherapy may be dispelled when modern high-energy neutron generators are put into clinical use. In particular, the better penetration and collimation possible with such machines will obviate many of the limitations and difficulties presently imposed on the Hammersmith workers, who conclude the book with a forcefully-stated argument that further trials be mounted using neutron generators capable of producing dose-distributions comparable to those achieved with conventional megavoltage photon machines: such trials, they suggest, would conclusively demonstrate the superiority of fast neutrons.

I have some sympathy with the authors' submissions but recall that the advent of megavoltage treatments did little to improve the best results achieved by their orthovoltage antecedents, but merely made treatment easier for patient and therapist alike. It seems likely that the "fast neutron saga" will continue for another 15 years at least, and future workers owe a great debt to the authors of this book, as well as to their many collaborators over the years.

M. L. SUTTON.

1981, *British Journal of Radiology*, 54, 606–614

Negative pion depth-dose profile examined by means of HeLa cell-survival curves

By D. H. Reading, B.Sc., Ph.D., M.Inst.P., M. A. Hynes, and W. S. Spinks

Rutherford and Appleton Laboratories, Chilton, Oxfordshire, OX11 0QX

and A. H. W. Nias, M.A., D.M., F.R.C.R.

Richard Dimbleby Department of Cancer Research, St. Thomas's Hospital Medical School, London SE1 7EH

(*Received May 1980 and in revised form January 1981*)

ABSTRACT

HeLa cells were irradiated at liquid nitrogen temperature with negative pions from Nimrod at the Rutherford Laboratory and then assayed for survival of colony-forming ability. Complete dose-response curves were obtained from repeated determinations at 14 different positions along the depth-dose profile and survival curves were fitted to the data by computer programme. A depth-damage profile was thus established in terms of the final slopes of these survival curves. This confirmed the expected RBE value of 1.84 at the ionization peak. Although a value of unity was found in the main plateau region, the "entrance" positions showed significantly higher values.

Negative pions offer a combination (Fowler, 1979; Skarsgard, 1979) of good dose and RBE localization (Raju *et al.*, 1978; Lloyd *et al.*, 1978) with low OER (Winston *et al.*, 1973; Prosser, 1980) and relative insensitivity to fractionation effects (Mill *et al.*, 1976b; Purrott, 1975). Negative pion radiotherapy is in progress at the Los Alamos Scientific Laboratory (Kligerman *et al.*, 1977) and is expected soon at Vancouver, Canada and Zürich, Switzerland. This study, in which HeLa cells were held in small ampoules at 1 cm spacing, has enabled the localization with depth to be determined for the pion beam at the Rutherford Laboratory where a considerable number of pre-clinical studies have been undertaken (Ellis *et al.*, 1976).

The main difficulty in obtaining such data has been the relatively low dose-rate obtainable. At low dose-rates the effect of radiation upon mammalian cells may be complicated by proliferation and recovery of the cell population if this is maintained at a normal temperature during the protracted period needed to deliver doses high enough to permit a reliable estimate of RBE (Fox and Nias, 1970). Previous studies (Nias and Ebert, 1969) with HeLa cells irradiated at liquid nitrogen temperature (−196°C) had shown that there was no change in response to irradiation by X or γ rays when the dose-rate was reduced from 1 Gy/min to 1 Gy/day. Under these conditions therefore both the complications of assaying the response of mammalian cells to protracted irradiation are avoided. Cells, once frozen, can be transported the long distances between a radiobiological laboratory (*e.g.*, Glasgow) and the Rutherford Laboratory and the pion exposure can be conducted over any convenient period, with any available dose-rate and even with interruptions. So long as the total absorbed dose has been measured, when the cells are thawed and plated to assay for survival of colony-forming ability, the cells respond as if they had received a single dose which can be considered to have been instantaneous. Using this technique we have previously determined the RBE of HeLa cells for both pions at the ionization peak and 14 MeV neutrons relative to 300 kV X rays (Nias *et al.*, 1974).

The present studies involved a systematic examination of variations in the shape of the dose-response curves for HeLa cells irradiated at 14 positions along the depth-dose profile including the "plateau" and the "peak" at doses up to 28 Gy. These data were sufficient to enable complete dose-response curves to be fitted using a computer programme (Gilbert, 1969). Some data were also obtained at two positions on the "tail" and off axis on the "peak". The dose-response to 250 kV X rays was also determined again, for comparison.

METHODS

Biological technique

HeLa cells were grown in monolayer culture, trypsinized and suspended at a concentration of 10^6/ml in Eagle's medium supplemented with 20% calf serum and 10% of the cryoprotective agent dimethyl sulphoxide. In order to ensure comparability between the more than 100 cell samples required for each of the series of irradiations, a large population of cells was pooled and 0.4 ml aliquots were placed in specially made 0.5 ml polypropylene ampoules. These were then frozen together under controlled conditions in an automatically programmed low-temperature refrigerator (GV Planer Ltd). The ampoules were transported to the Rutherford Laboratory in dry ice and on receipt were stored in liquid nitrogen. After irradiation they were returned to Glasgow in a similar manner.

At convenient intervals, random batches were rapidly thawed by plunging the ampoules in water at 37°C. The thawed cells were immediately diluted in culture medium and counted electronically. Two further successive tenfold dilutions were made and three replicate 5 ml volumes at each dilution were inoculated into T30 plastic bottles on which the clones were allowed to grow for ten days before fixation and staining. In this way a suitable clone density was achieved without the experimenter being aware of the history of the sample. No lethally irradiated cells were added. Scoring was based on clone forming ability as has been described previously (Nias and Ebert, 1969).

The irradiation facility

The beam line has been described by Perry and Hynes (1971). Pions were produced at the Rutherford Laboratory by the interaction of protons with momentum 8 GeV/c (7 GeV energy) from the synchrotron Nimrod with atomic nuclei in a copper target.

They were collected in a quadrupole pair, momentum and charge selected by a bending magnet and focused onto the irradiation volume. The present experiments were carried out with a pion beam nominally 160 MeV/c (74 MeV) and a momentum spread of 13% full width half maximum (FWHM). This produced a peak to plateau dose ratio of about 1.4 as shown in Fig. 1. The beam size was 5 cm FWHM; 2.2 cm at the 80% level.

The results presented were obtained in four separate sessions between 1974 and 1977 inclusive, using various copper targets with lengths of 4 to 10 cm. The smaller lengths were as required by other users. Owing to this variation, and changes in the proton beam focusing and steering, detailed dosimetry was undertaken for each condition. Dose rates varied between 0.3 and 1.2 Gy per hour. This includes lepton contamination comprising 10% muons and 12 to 15% electrons, depending on the target, which contributed 1 and 4% respectively of the dose at the peak when allowance was made for different spatial and momentum distributions (Ellis *et al.*, 1976; Paler *et al.*, 1978).

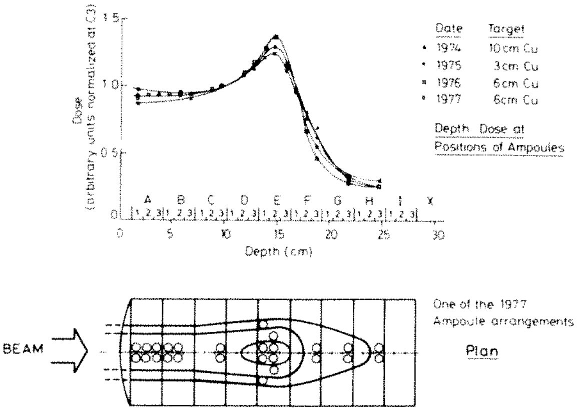


FIG. 1.

Depth-dose profiles for the four series of exposures (above) and one of the 1977 ampoule arrangements showing the 20, 50 and 80% dose contours.

A stainless-steel vacuum cryostat with Mylar beam-entrance windows held the phantom submerged in liquid nitrogen. The ampoules were positioned in pairs in a horizontal stack of plastic discs of composition $C_{61}O_{20}N_{11}Cl_1H_{113}$, density 1.12 g/cm^3. An initial disc which held no ampoules was made of a fluorinated hydrocarbon (PTFE, 2.2 g/cm^3) and was shaped to the contour of the window, 1.2 cm thick at the centre. In order to minimize the effects of air gaps in the ampoules the phantom was sloped by 2°, with the entrance higher. An arrangement used for a part of the experiment is given on the bottom of Fig. 1.

The comparison with conventional radiation was done using 250 kV X rays, 2 mm Cu HVL at a dose rate of 1 Gy/min. Cells of the 1977 batch were held in their ampoules in a glass Dewar containing a polythene insert immersed in liquid nitrogen.

Dosimetry

The pion dose was measured within the phantom with a 0.2 c.c. air-equivalent thimble ion chamber which, surrounded by a plastic sheath, fitted into the same holes as did the ampoules. Dummy ampoules were placed in the other holes during the measurement and the liquid nitrogen replaced with water at room temperature. The depth-dose curves in the upper part of Fig. 1 differ from other published curves (Lloyd *et al.*, 1975; Mill *et al.*, 1976a) because of the non-axial locus and because of air spaces in the upstream ampoules. It further differs from that in our earlier paper (Nias *et al.*, 1974) since in that experiment the cells remained at the same position relative to the beam elements and different depths were obtained by varying the amount of material placed in front.

The ion chamber was calibrated by placing it mid-way between two ^{60}Co γ sources using a 0.5 cm Perspex build-up cap. Dose–exposure constants of 13.2 R/mCih at 1 cm and 1.03 R/rad were used to obtain ^{60}Co equivalent rad in water (9.63×10^{-17} Gy/Bq sec at 1 m). The inverse-square law was well satisfied and the result agreed to 3% with an independent calibration by the NRPB Harwell using ^{137}Cs. Standard corrections were applied for temperature and pressure but no further factors were applied for kerma, W value or stopping power variations of the pion products, as the uncertainties on such corrections exceed the best estimate of the corrections.

In this work, the quoted dose refers to that averaged over the chamber volume when centred on the cell positions in each ampoule. The linear displacement of the effective centre of the ion chamber is calculated to be −2.5 mm for a unidirectional radiation field. Such a displacement would cause an underestimation of 2% just before the peak (at D and El) and an overestimate after the peak reaching 8% at F2 falling to 1% at H3. Smaller effects arise from the change of dose distribution due to the contraction of the phantom on cooling and the replacement of water by liquid nitrogen. These are a quarter the magnitude and have been ignored.

During the time between calibration of the ion chamber and its use in the beam its response was checked with a portable ^{90}Sr rig (Nuclear Enterprises type 2503). A transmission ion chamber served as a monitor during the cell exposures.

The X-ray dose was measured using LiF dosimetry at room temperature, referred to a Baldwin secondary standard dosimeter.

RESULTS

Survival curves at each of the sites at which we have sufficient data to make a fit (two successful ampoules from separate irradiations at four different doses) are given in Fig. 2. Each point represents the relative cloning ability compared to control ampoules of the same batch which were transported and placed in the phantom but not irradiated. The error bars indicate the standard error of the mean of the surviving fractions from the repeated determinations at each dose.

The data were analysed using the computer program of Gilbert (1969) which provides figures for the shape of a Puck-type cell-survival curve in terms of its exponential slope and extrapolation number. The data from the repeated experiments were combined and weighted according to the number of observations (*i.e.*, total number of clones) at each dose at each site. Calculations were made to determine the parameters of the survival curve for each site separately. The extrapolation numbers obtained by these separate calculations were not significantly different. The experimental data were therefore used for a further calculation, assuming

TABLE I

NUMERICAL RESULTS

Position	A_1	A_2	A_3	B_1	B_2	B_3	C_3	D_3	E_1	E_2	E_3	F_1	F_2	F_3	X-ray
Depth (cm)	1.7	2.7	3.7	4.7	3.7	6.7	9.7	12.7	13.7	14.7	15.7	16.7	17.7	18.7	—
Depth (g/cm^{-2})	3.2	4.3	5.4	6.6	7.7	8.8	12.2	15.5	16.6	17.8	18.9	20.0	21.1	22.2	—
Dose relative to C_3 (1976)*	0.91	0.92	0.93	0.93	0.93	0.95	1.0	1.18	1.29	1.37	1.17	0.98	0.67	0.46	—
D_0 (Gy)	4.24	4.17	4.59	4.64	4.96	5.52	3.91	3.58	3.25	3.00	3.14	3.46	3.51	5.27	6.50
± SE	0.29	0.39	0.39	0.39	0.41	0.47	0.27	0.30	0.30	0.25	—	0.28	0.34	0.49	0.71
RBE	1.53	1.56	1.42	1.40	1.31	1.18	1.66	1.82	2.00	2.17	2.07	1.88	1.85	1.23	1.00

*For the degree of variation between the different exposures combined in this experiment see Fig. 1.

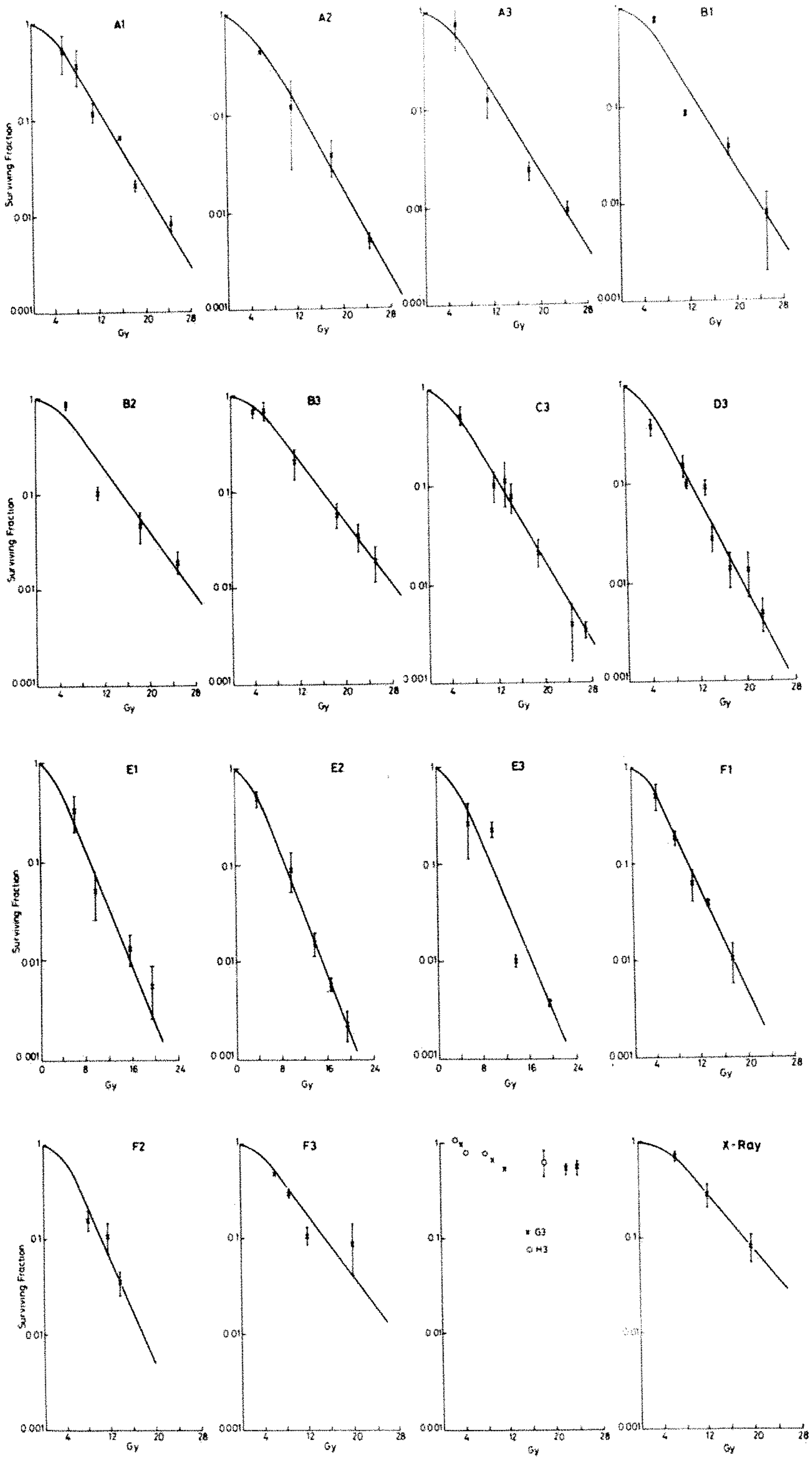


FIG. 2.

Dose-survival curves of HeLa cells irradiated by pions at various depths and by X rays.

survival curves of the same shape with only a dose modifying factor between the different sites in the pion beam. The common extrapolation number was 1.91 ± 0.09 (compared to 2.06 ± 0.23 in our previous determinations (Nias *et al.*, 1974)). The final slope of the curves is the negative exponential term D_0 which dominates at high doses.

The survival curve for X-irradiated cells is also shown in Fig. 2. These limited data were sufficient to confirm that the radiosensitivity of the HeLa cells, $D_0=6.50\pm0.71$ Gy, had not changed significantly since our previous determination ($D_0=6.77\pm0.31$ Gy). RBE values were obtained by a simple comparison of D_0 values and are listed in Table I together with corresponding depths and relative doses.

The RBE for the pion beam at position B3 (6.7 cm depth) is 1.18 (with reference to X rays). If this position in the beam is taken as the "plateau" then the peak to plateau ratio can be derived by comparing the D_0 values for pions at positions E2 and B3 and a value of 1.84 is obtained (compared to 1.86 in our previous report). A ratio can also be obtained between the "entrance" and the plateau by comparing the D_0 values at positions A1 and B3, giving a value of 1.30.

As the above analysis was our first priority we did not routinely measure the response over the entire phantom for a given number of incident pions. Cells were usually removed early from the peak position, and kept in place on the tail so as to obtain similar survival levels. There were exceptions when ampoules were simultaneously exposed at a significant number of depths and then removed. These are given in Fig. 3 together with the relevant dose profile. The error bars are determined as in Fig. 2, where data allow, or else are of a similar magnitude. The 1977 data are put with the 1976 data as they only cover the plateau region.

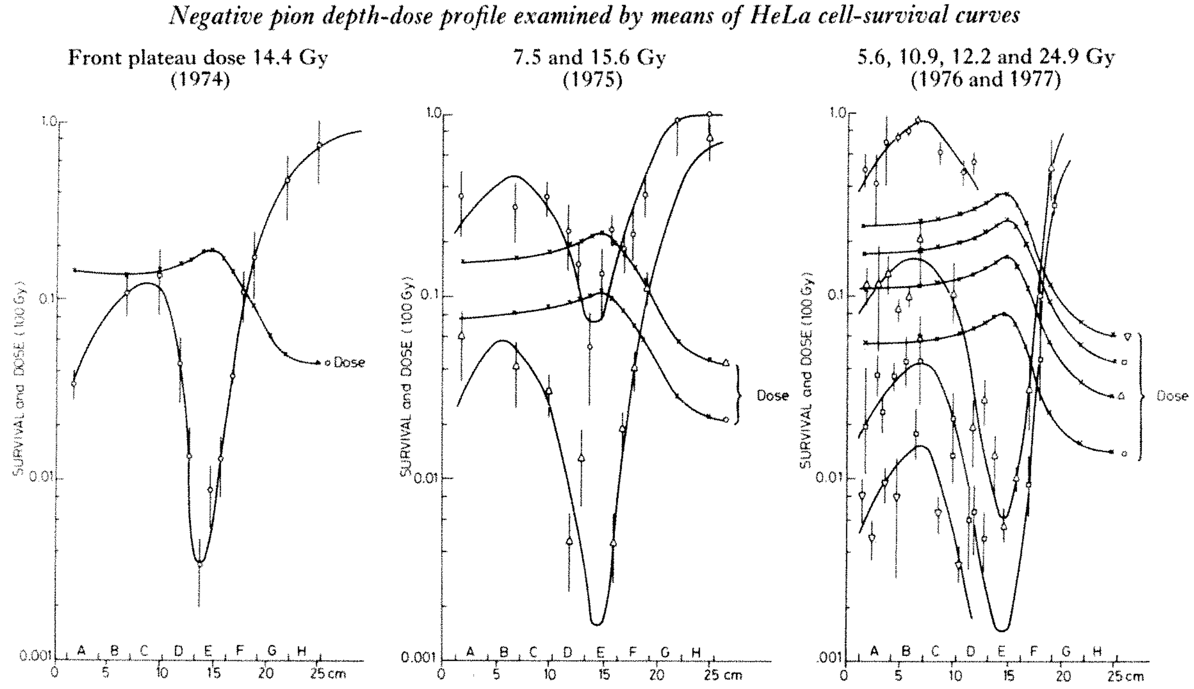
At positions well away from the beam axis, it is expected that the beam quality may alter due to the different spatial distributions of the lepton contaminants and the higher proportion of pion-induced dose from neutrons and fast products. Off-axis exposures were taken at the peak positions E1 (sideways) and E2 (sideways-up). At these positions the dose had fallen to 37% and 43%, respectively, of the dose on axis. The survival was 7.0 and 0.9 times higher than the expected survival at these depths and doses. Allowance has been made for the 2:1 dose variation over the E2 off-axis sample. This indicates RBE values of 1.3 and 2.3 off axis (compared with RBE values of 2.0 and 2.17 for positions E1 and E2 on axis; Table I). The data at these two off-axis positions give some indication that at the edge of a narrow pion beam in the peak region the biological effect falls off faster than the dose.

Discussion

Dose is quoted in terms of the response of the ion chamber to γ rays. Corrections to be applied because of the nature of pion radiation could be as large as 20% and variable over the phantom. The pion W value, the energy required to liberate one ion pair, has been variously estimated as 1.03 (Perris *et al.*, 1978) and 1.01 (Shortt, 1979) times that of electrons. Further uncertainties are introduced by the ion chamber not being a perfect Bragg-Gray cavity and not being tissue equivalent, lacking oxygen and hydrogen. The ratio of the stopping power of carbon to wet tissue for the pions and most of the products of their interactions is 0.9 (ICRU 1978; Bichsel 1968). The energy released to charged fragments at a pion interaction accounts for half the dose in the peak region. A theoretical estimate by Guthrie (1968) of the ratio from carbon and oxygen is 0.82. A measurement by Fowler and Mays (1967) using wet and dry emulsion found 1.05±0.13. Shortt (1979) reports a determination by Amols *et al.*, (1979) using a counter technique of 2.0±0.7. Perris *et al.* (1978) found the ratio for C: muscle equivalent solution: O to be 1.04±0.19: 1.13±0.19: 1. The contribution from interactions in flight on the plateau is largely unknown. It probably accounts for 25% of the dose there and includes fast low LET products. Only one limited experiment has been reported (Perris *et al.*, 1978). A direct comparison with a neutron tissue-equivalent ion chamber and tests in which spherical shells of polythene replaced water about the ion chamber produced negligible effect (Smith and Telling, 1975).

In these studies with frozen HeLa cells, pions are shown to have the expected localization in radiation quality (high RBE) as well as in dose. This is indicated in the survival-depth curves, Fig. 3, and the D_0 and RBE values obtained from the survival-dose curves as shown in Figs. 4 and 5 and Table I. These data are in agreement with our previous observations of frozen HeLa cells irradiated with pions at the ionization peak ($D_0=3.64\pm0.24$ Gy) and with 300 kV X rays ($D_0=6.77\pm0.31$ Gy) which indicated an RBE of 1.86 (Nias *et al.*, 1974). We had also observed an RBE value of 1 in the plateau region which is also in agreement with the current data at the 6.7 cm position (Table I).

Other workers have found similar values for RBE at the ionization peak of the Nimrod pion beam. Perhaps the more useful parameter, for clinical



Negative pion depth-dose profile examined by means of HeLa cell-survival curves

Front plateau dose 14.4 Gy (1974)

7.5 and 15.6 Gy (1975)

5.6, 10.9, 12.2 and 24.9 Gy (1976 and 1977)

FIG. 3.

Survival of HeLa cells as a function of depth in a phantom. Each curve shows the response of cells simultaneously exposed to an incident pion beam with the depth-dose distribution illustrated. Results are shown from all four experimental sessions.

purposes at least, is the peak to plateau ratio in terms of RBE values. Our present data show a maximum of 1.84 if the 6.7 cm position is chosen to represent the plateau. Most other workers either use a similar position to this or do not specify the precise position in the plateau. (The relative paucity of data from "surface" positions is discussed below.) The peak to plateau ratio for chromosomal damage in human peripheral blood lymphocytes was 1.8 (Lloyd *et al.*, 1975) but reduced to 1.5 with the sort of broader peak more applicable to clinical practice (Lloyd *et al.*, 1978); for *Vicia faba* root growth it was about 2 (Winston *et al.*, 1973); for the survival of HeLa cells irradiated at room temperature it was 1.4 (Mill *et al.*, 1976a). With the Los Alamos pion beam the ratio for V79 cell survival was 1.5 (Raju *et al.*, 1978); with the TRIUMF beam the ratio for CHO cell survival was also 1.5 (Skarsgard *et al.*, 1977); with the SIN beam the ratio for V79 cell survival was 1.8 for monolayer cultures and 1.5 for spheroids (Dertinger *et al.*, 1976) for a 5 cm peak width.

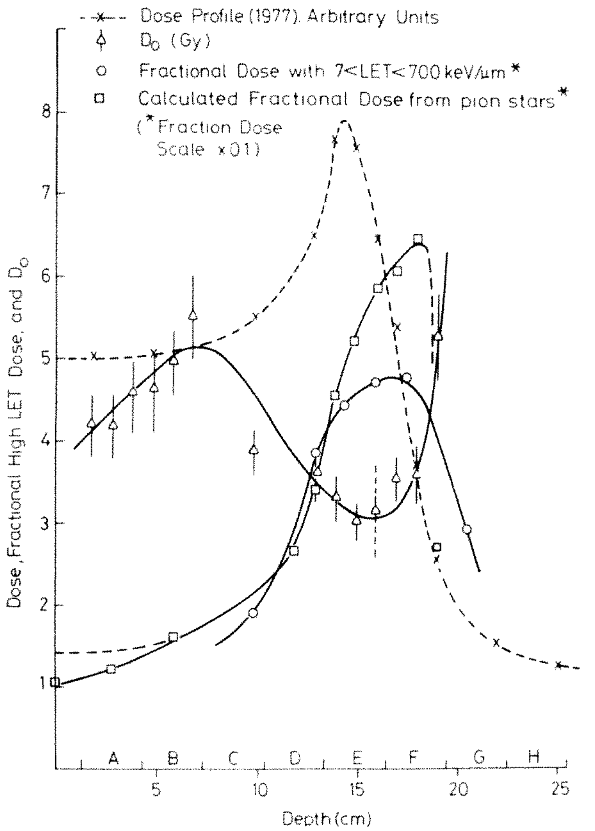


FIG. 4.

The variation with depth of dose and D_0 as determined in this experiment compared with the fraction of the dose with high LET and a theoretical estimate of the fraction of the dose due to 35 MeV per pion star.

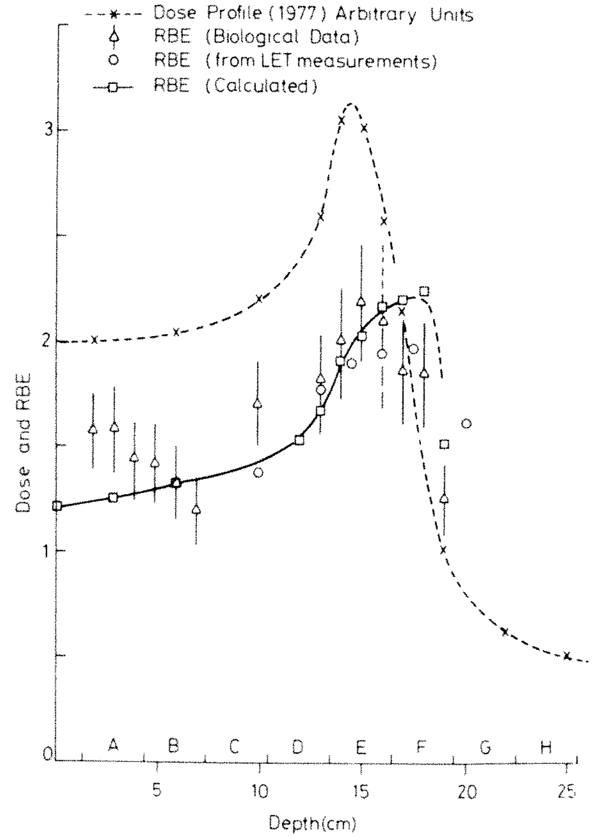


Fig. 5.

The variation with depth of dose and RBE as determined in this experiment compared to RBE as computed from LET measurements and from the pion star distribution.

It is instructive to compare the observed D_0 and RBE with calculated values based on the physical characteristics of the beam line and radiation field. This is done on Figs. 4 and 5.

On Fig. 4 the D_0 distribution is shown together with the fraction of dose with a high LET (between 7 and 700 keV/μm) as measured with an EG&G Rossi counter in water (Lewis, 1979). A separate comparison between depths of 2 g/cm^2 and 6.5 g/cm^2 showed no significant difference. At the peak depth an enhanced low LET contribution was observed when the counter was moved off axis. There is also shown on Fig. 4 a theoretical curve of the fraction of the dose with high LET. This is from a Monte Carlo calculation which tracked pions through the beam line elements so as to obtain the momentum distribution incident on the phantom, and hence the distribution of pion stars. High LET in this instance is defined as 35 MeV per pion star, the 30 MeV from charged products (Fowler and Mays, 1967; Mechtersheimer *et al.*, 1978) and 5 MeV deposited by the absorption of emitted neutrons. This value is reasonable for pion interactions in flight as well as at rest, for in flight the increased energy of secondary products adds a low LET component. This is taken as a third of the pion's kinetic energy.

Both these fractional dose curves have been normalized with depth according to the measured or calculated position of the dose peak, as they were obtained with different phantoms.

It is seen that D_0 and the fractional dose curves have similar widths and reach extreme values 2–3 cm beyond the dose peak. At the peak the greater fractional dose derived from the Monte Carlo calculation is consistent with the inclusion of dose due to products with LET < 7 keV/μm.

The RBE is taken as the ratio of D_0 values and may thus be considered independent of dose. This allows us to say that the pion dose is equivalent to a low LET radiation equal to the low LET component of the pion dose plus the high LET component multiplied by an arbitrary RBE. Thus

$$\text{RBE (pion)} = \frac{\text{low LET equivalent dose}}{\text{pion dose}} = \frac{\text{Dose (low LET)} + \text{Dose (high LET)} \times \text{RBE (high LET)}}{\text{Dose (low LET)} + \text{Dose (high LET)}}$$

Taking the value 3.0 for RBE (high LET), theoretical values of RBE (pion) have been calculated as a function of depth using both the experimental and theoretical estimates of the fraction of dose with high LET. These values are plotted on Fig. 5 together with the measured RBE and dose. There is fair agreement, with all the determinations of RBE reaching high values at the dose peak and staying high for 4 cm thereafter.

The experimental RBE has an enhancement near the surface which decreases with depth, in contrast to the predictions. It should be noted that we have not investigated the RBE right at the surface as our first sample mid-line was at 1.7 cm (3.2 g/cm^2). An effect near the surface in this beam has been reported by Winston *et al.* (1974) and Lloyd *et al.* (1978), though another recent experiment by Lloyd (1981) does not support it. The surface region has not been explored in any other pion beam. Raju *et al.* (1978), for example, state that the "entrance" region in their studies was very close to the proximal side of the peak.

There are several factors which may produce an enhanced effect near the surface, but none of the magnitude indicated. The pion cross-section decreases with depth in the phantom (Binon *et al.*, 1970; Clough *et al.*, 1973; Doss *et al.*, 1976) and is allowed for in our calculations. Any multiply charged particles in the beam with the design momentum of the beam line would have too short a range. Incident neutrons have been measured and give an estimated dose contribution of $< 1\%$ at the peak (Ellis *et al.*, 1976). The initial PTFE disc might have produced higher LET products, but none were observed using the Rossi counter (Lewis, 1979). Finally, an additional high LET component would be generated by secondary products and scattered pions from the flange of the vacuum window of the phantom, but only 10% of the pion beam failed to clear this collimator.

Whatever the explanation may be, we draw attention to this enhanced effect at the surface in our experimental set-up since the particular circumstances that produce it may possibly be reproduced in certain clinical pion facilities. In such a case, an increased skin or mucosal reaction may be noted and it should then be possible to modify the treatment portal if this reaction is deemed unacceptable. The peak to plateau RBE ratio of 1.84 would otherwise be reduced to a peak to "entrance" ratio of 1.41 and this would reduce the clinical advantage of the dose distribution and effect of such a pion beam.

Finally, we draw the reader's attention to our data taken on the tail, well beyond the ionization peak (Fig. 2.). It is seen that D_0 is not well determined, but is anomalously low. We note that the cells had to stay in the phantom for up to three weeks during the irradiation but since they were maintained in liquid nitrogen this should not have influenced the response. The measured dose rates were low (0.05 to 0.2 Gy/h) adjacent to a much higher dose rate region, and this might have given rise to errors in dosimetry. We have no indication that any such factors did, in fact, contribute to a false value.

Conclusion

HeLa cells have been subjected to the radiation field of negative pi-mesons at representative positions in a phantom and at a large range of doses. Significant enhancement of effect was seen at the peak region with an RBE of 2.17, compared to the plateau value of 1.18 as listed in Table I. There were indications of increased effect near the surface although this has no theoretical support. The radiation beyond the peak produces little damage consistent with an RBE of unity or lower.

This experiment adds to the growing body of data which indicates that negative pions have great promise for the treatment of cancer.

Acknowledgments

The authors wish to thank Mrs. Sheila McEwan for her work with the cell cultures and also Dr. C. A. Lewis for help during the irradiations and for taking special microdosimetric measurements. The operations staff at Nimrod kept a special eye on this experiment, and without their active co-operation the long running periods would have been impossible.

REFERENCES

Amols, H. I., Büche, G., Kluge, W., Matthäy, H., Moline, A., Münchmeyer, D. and Randoll, H., 1979. Measurements of energy spectrum of charged particles emitted following the absorption of stopped pions on oxygen containing compounds and in calcium. *S.I.N. Newsletter, No. 11*, 67–69.

Bichsel, H., 1968. Charged particle interactions. In *Radiation Dosimetry Fundamentals*, Ed. F. H. Attix and W. C. Roesch, vol. 1., chapter 4 (Academic Press, New York).

Binon, F., Duteil, P., Garron, J. P., Gorres, J., Hugon, L., Peigneux, J. P., Schmit, C., Spighel, M. and Stroot, J. P., 1970. Scattering of negative pion on carbon. *Nuclear Physics, B17*, 168–188.

Clough, A. S., Turner, G. K., Allardyce, B. W., Batty, C. J., Baugh, D. J., McDonald, J. D., Riddle, R. A. J., Watson, L. H., Cage, M. E., Pyle, G. T., and Squire, G. T. A., 1973. Coulomb effects in π^+ and π^- – C total cross sections. *Physics Letters, 43B*, 476–478.

Dertinger, H., Lücke-Huhle, C., Schlag, H. and Weibezahn, K. F., 1976. Negative pion irradiation of mammalian cells. *International Journal of Radiation Biology, 29*, 271–277.

Doss, K. G. R., Dytman, S. A. and Silbar, R. R., 1976. A compilation of pion absorption data. *Conference on Meson-Nuclear Physics. American Institute of Physics Conference Proceedings, No. 33*, 344–345.

Ellis, R. E., Lindop, P. J., Coggle, J. E. and Fraser, G., 1976. Radiobiological work using a negative pion beam at the Rutherford Laboratory (Rutherford Laboratory, RL–76–092 Rev 1.)

Fowler, J. F., 1979. New horizons in radiation oncology. *British Journal of Radiology, 52*, 523–535.

Fowler, P. H. and Mayes, V. M., 1967. The capture of π^- mesons in oxygen and in other nuclei. *Proceedings of the Physics Society, 92*, 377–389.

Fox, M. and Nias, A. H. W., 1970. The influence of recovery from sublethal damage on the response of cells to protracted irradiation at low dose-rate. *Current Topics in Radiation Research Quarterly, 7*, 71–103.

Gilbert, C. W., 1969. Computer programmes for fitting Puck and probit survival curves. *International Journal of Radiation Biology, 16*, 323–332.

Guthrie, M. P., Alsmiller, R. G. Jnr. and Bertini, H. W., 1968. Calculation of the capture of negative pions in light elements and comparison with experiments pertaining to cancer radiotherapy. *Nuclear Instruments and Methods, 66*, 29–36.

International Commission on Radiation Units and Measurements, 1978. Basic aspects of high energy particle interactions and radiation dosimetry. ICRU Report 28. (International Commission on Radiation Units and Measurement, Washington, DC)

Kligerman, M. M., Smith, A., Yuhas, J. M., Wilson, S., Sternhagen, C. J., Helland, J. A. and Sala, J. M., 1977. The relative biological effectiveness of pions in the acute response of human skin. *International Journal of Radiation Oncology, Biology, Physics, 3*, 335–339.

Lewis, C. A., 1979. An investigation of the linear energy transfer distribution in a beam of negative pi-mesons. *Ph.D. Thesis, University of Leeds, reprint RL–79–057.*

Lloyd, D. C. 1981. In preparation.

Lloyd, D. C., Purrott, R. J., Dolphin, G. W. and

Reading, D. H., 1975. An investigation of the characteristics of a negative pion beam by means of induced chromosome aberrations in human peripheral blood lymphocytes. *International Journal of Radiation Biology, 27,* 223–236.

Lloyd, D. C., Reading, D. H., Purrott, R. J., Hynes, M. A., Spinks, W. S. and Stephenson, B. D., 1978. Expansion of a negative pi-meson peak to cover a range of depths for radiotherapy. *British Journal of Radiology, 51,* 41–45.

Mechtersheimer, G., Büche, G., Klein, U., Kluge, W., Matthay, H., Münchmeyer, D. and Moline, A., 1978. Measurements of energy spectrum of charged particles emitted after the absorption of stopped negative pions in carbon. *Physics Letters (B). 73,* 115–118.

Mill, A. J., Lewis, J. D. and Hall, W. S., 1976a. Response of HeLa cells to irradiation with π^- mesons. *British Journal of Radiology, 49,* 166–171.

1976b. Recovery in mammalian cells irradiated with a beam of π^- mesons. *British Journal of Radiology, 49,* 357–359.

Nias, A. H. W. and Ebert, M., 1969. Effects of single and continuous irradiation of HeLa cells at −196°C. *International Journal of Radiation Biology, 16,* 31–41.

Nias, A. H. W., Greene, D., Major, D., Perry, D. R. and Reading, D. H., 1974. Determination of RBE values for fast neutrons and negative π mesons using frozen HeLa cells. *British Journal of Radiology, 47,* 800–804.

Paler, K., Arnison, G. and Cameron, W., 1978. In *Particle Physics Experiments,* (Rutherford Laboratory, RL–79–018), p. 177.

Perris, A. G., Smith, F. A. and Perry, D. R., 1978. Charged particles emission from the capture of negative pions: energy spectra, LET distributions and W-value. *Physics in Medicine and Biology, 23,* 217–234.

Perry, D. R. and Hynes, M. A., 1971. A pion beam for radiological and dosimetric studies using a proton synchrotron external target. *Proceedings of International Conference on Protection against Acceleration and Spare Radiations* (CERN, Geneva) 71–16, *vol. 1,* pp. 220–228.

Prosser, J. S. and Priseman, S. J., 1980. The induction of chromosome negative pi-mesons under conditions of anoxia and oxygenation. *Experientia, 36,* 869–870.

Purrott, J., 1975. Chromosome aberration yield in human lymphocytes exposed to fractionated doses of negative π mesons. *International Journal of Radiation Biology, 28,* 599–602.

Raju, M. R., Amols, H. I., Bain, E., Carpenter, S. G., Cox, R. A. and Robertson, J. B., 1978. A heavy particle comparative study: OER and RBE. *British Journal of Radiology, 51,* 712–719.

Shortt, K. R., 1979. The absolute dosimetry of negative pions. (Ph.D. Thesis, University of British Columbia).

Skarsgard, L. D., 1979. Biological properties of pions. In *Particle Radiobiology and Tumour Therapy,* Symposium, Tokyo, May 1979 (International Atomic Energy Authority, Vienna)

Skarsgard, L. D., Henkelman, R. M., Lam, G. K. Y., Harrison, R. W. and Palcic, B., 1977. Physical and radiobiological properties of the negative pi-meson beam at TRIUMF. In *Radiobiological Research and Radiotherapy,* IAEA, II (International Atomic Energy Agency, Vienna), pp. 87–98.

Smith, J. R. and Telling, F. M., Ed., 1975. The Work of the Rutherford Laboratory 1974, pp. 92–93.

Winston, B. M., Berry, R. J. and Perry, D. R., 1973. Response of *Vicia faba* to irradiation with a beam of negative pi-mesons, under aerobic and hypoxic conditions. *British Journal of Radiology, 46,* 541–547.

Winston, B. M., Berry, R. J., Perry, D. R. and Reading, D. H., 1974. Effects of the radiation at the entrance point of a negative pi-meson beam. *British Journal of Radiology, 47,* 201–203.

Book review

Cellular Radiobiology. By Tikvah Alper, pp.320, 1979 (Cambridge University Press), £18·00 hardback; £5·95 paperback.
ISBN 0-521-22411

Considering the importance of the subject and the scientific effort devoted to it, there are surprisingly few comprehensive books on radiobiology. This latest volume, as the title suggests, confines itself to the response of cells to radiation, with only a short section on *in vivo* radiobiology at the end. The author has had a distinguished career in radiobiology and this work has a recognisably personal approach to the subject.

In concept it is a teaching book and the reader is led through the 17 chapters with new concepts being introduced only when it is appropriate to explain them in full. This technique does not always make for the smoothest reading, however. The book is particularly strong in the chapters on target theory and cell-survival-curve shapes (Chapters 4 and 5). In this respect it is the most up-to-date and definitive work in these areas and will no doubt become the standard reference source for many years to come.

However, the book is not without errors that should have been spotted in proof reading and, while many of them are fairly obvious, there is a large concentration in Chapter 6 which could confuse all but the brighter student. For example, in the appendix of derivations (p. 69) there are unnecessary conceptual complications and about nine misprints, while p. 42 contains (i) a misquote of published data and (ii) in note (e) "anoxic" has been used instead of "oxic".

On balance, the good points outweigh the less good ones and I recommend this volume not only to the appropriate scientific libraries but as an addition to the personal collections of radiobiologists.

M. Fielden.

1981, *British Journal of Radiology*, 54, 615–621

The effects of NMR exposure on living organisms.

I. A microbial assay

By A. Thomas, B.Sc., and *P. G. Morris, M.A., Ph.D.

Departments of Genetics and Physics, University of Nottingham, University Park, Nottingham NG7 2RD

(*Received July 1980*)

ABSTRACT

Various bacterial strains have been exposed to a homogeneous magnetic field of 1 Tesla and to the conditions found in an NMR imaging experiment of the type used in a recent abdominal scan (Mansfield *et al.*, 1978). No mutagenic or lethal effects were observed. The activity of the bacterial enzyme β-galactosidase was also found to be independent of the applied magnetic field.

Nuclear magnetic resonance (NMR) spectroscopy is a powerful analytical tool used routinely for the determination of sample compositions, for the elucidation of molecular structures and for the study of molecular motions. Whereas its importance to the organic chemist is paramount, the medical application to date has been limited, being restricted by the small sample volume (1 cm^3) and lack of spatial discrimination. Nevertheless, some progress has been made in this area, for instance the detection of malignancy in biopsy samples (Damadian, 1971; Koutcher *et al.*, 1978) and the metabolic studies of perfused organs such as the heart and liver (Gadian, 1977).

The development of NMR imaging techniques (Lauterbur, 1973; Mansfield and Grannell, 1973) and their subsequent extension to intermediate (Hinshaw *et al.*, 1977) and whole-body dimensions (Damadian *et al.*, 1977; Mansfield *et al.*, 1978; Mallard *et al.*, 1980; Moore and Holland, 1980) encourages us to believe that medical imaging by NMR will become a reality within the next few years.

A major attraction of the technique is the apparent lack of associated hazard; power levels are in general low and there is no ionizing radiation. Nevertheless, with the increasing number of experiments on human subjects, we believe that the time has come for a careful appraisal of potential health hazards using modern screening techniques such as those of Ames (1971). (Although these were developed for chemical mutagens they can equally well be used for physical agents.)

In the present study a series of exploratory experiments were performed in which bacterial strains were exposed to conditions comparable with the abdominal proton NMR scan referred to above (Mansfield *et al.*, 1978).

It is likely that NMR imaging will be applied to other nuclei, for instance ^{31}P, which will require the use of larger magnetic fields. A second series of experiments was therefore performed in which the effects of a 1 tesla magnetic field on the same series of bacterial strains and an enzyme system (β-galactosidase) were investigated.

This study is the first in a series of investigations into possible hazards associated with NMR imaging. The second, dealing with human white blood cells, appears as the subsequent paper in this issue (Cooke and Morris, 1981). Other experiments on higher organisms are at present under way in this laboratory and will be reported at a later date.

POTENTIAL HAZARDS OF NMR IMAGING

The principal features of an NMR imaging experiment which are potential health hazards are: the static magnetic field, the radiofrequency power and the time-dependent field gradients. The relative importance of these effects has been recently reviewed (Budinger, 1979) and only a brief discussion is therefore given below. It is conceivable that effects may arise from the combination of some or all of the above experimental features, hence our decision to expose the screens to a full imaging experiment.

Static magnetic fields

The literature on homogeneous magnetic field effects is extensive and often contradictory (Barnothy, 1964, 1969; Tenforde, 1978).

The predominant effects will probably be interactions with the anisotropic magnetic susceptibility of large molecules resulting in a change of conformation or orientation which may affect enzyme activity. Minor effects may be interactions with paramagnetic centres which could be present naturally or occur as reaction intermediates. Finally, any ferromagnetic material which may form part of a "magnetic" guidance system in certain organisms (Blakemore *et al.*, 1979) will obviously show a strong effect.

---

*Present address and address for reprints: NMR Centre, National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA.

Budinger (1979) concludes from his survey however that "no substantial biological evidence exists for magnetic field effects below 0.5 T".

Radio-frequency power

At the power levels currently proposed for NMR imaging there is no evidence for any effect in the human body other than radiofrequency heating. Even this effect represents only a small fraction of the heating by the basal metabolic rate and is thus well within the current US safety standard.

Time-dependent magnetic fields

Most NMR imaging methods involve oscillatory or switched magnetic field gradients which induce EMFs and therefore currents in the conducting regions of the body. Budinger (1979) estimates, on the basis of a simple model, that a magnetic field varying at 1 T s^{-1} will give rise to a current density of 1 μA cm^{-2}. Based on the threshold levels for observation of phosphenes and other physiological effects, it is concluded that field variations of 3 T s^{-1} or less should not have a significant biological effect. This figure, however, may well depend on the detailed time variation of the magnetic field as well as on the peak value of dB/dt.

EXPERIMENTAL DETAILS

High field

A homogeneous magnetic field of 1 T was produced by a Varian 3400 electromagnet. The bacterial strains were exposed for either one or five hours at a temperature of 27±3°C, whereas for an enzyme study exposure was for a period of 40 minutes at a temperature of 26±0.25°C.

NMR imaging exposure

The bacterial strains were exposed to conditions similar to those experienced in a whole-body NMR scan (Mansfield *et al.*, 1978). Details of the line scanning method and of the apparatus are available elsewhere (Mansfield *et al.*, 1976; Morris *et al.*, 1979) and therefore only the features representing possible biological hazards are described below.

The experiment consisted of two stages: a "setting-up" period of approximately half-an-hour when only the static magnetic field was applied, and a period of either 40 minutes or five hours (see individual experiments for details) during which the full NMR imaging experiment was performed. The mean temperature during the experiment was 30±3°C.

Experimental details were as follows:

Static magnetic field: 0.09395 T

Radiofrequency transmitter power: peak 4.35 W, mean 0.097 W. (Mean power absorbed by the torso in an abdominal scan is estimated as about 0.03 W).

Switched field gradients*: switching occurs approximately 9 times s^{-1}. Maximum dB/dt during switching is approximately 1 T s^{-1}.

BIOLOGICAL TEST SYSTEM AND RESULTS

1. *Survival of* E. coli

This experiment was designed to test the direct effect of an NMR imaging experiment on the survival of bacterial cells using media and culture methods described previously by Low (1973a; b). Standard aseptic techniques were used throughout.

An exponential culture of *Escherichia coli*, strain AB1157 (Bachman, 1972), was grown in Luria Broth (LB) to an optical density (OD) of 0.4 (650 nm) which corresponds to about 2×10^8 cells ml^{-1}. Dilutions were made in 56/2 buffer (a minimal salts buffer consisting of KH_2PO_4, Na_2HPO_4, $MgSO_4$ $(NH_4)_2SO_4$, $Ca(NO_3)_2$ and $FeSO_4$ dissolved in distilled water) by 10^{-5} and 0.01 ml aliquots were applied to LB agar (1.5%) plates (90 mm plastic microbial petri dishes). Nine plates were prepared, each carrying 16 drops of identical dilutions of the same culture.

In sets of three the plates were:

B1 left on the bench as a control;
B2 subjected to NMR imaging for 40 minutes;
B3 subjected to a 1 T static field for one hour.

If the viability is unaffected by the treatment, then each cell should have the ability to form a colony. The plates were therefore incubated at 35°C for 12 hours and the number of bacterial colonies within each drop was scored.

Results and analysis. The colony scores are shown in the upper part of Table I. Each individual figure refers to the number of colonies within an aliquot and each block of 16 represents a plate.

In order to determine whether there are any differences between the numbers of colonies on the plates a two-way analysis of variance was carried out. This is shown in the lower part of Table I and shows that, although the repeat (A) and treatment (B) terms show no significance, the interactive term (AB) is significant at the 5% level. In order to investigate further the source of this variance, each

---

*In the case of the bacteriophage induction assay an echo-planar imaging (Mansfield and Pykett, 1978; Mansfield *et al.* 1980) exposure of five hours was used. The gradients were switched approximately 64 times s^{-1} with a maximum dB/dT of around 12 T s^{-1}. Static magnetic field and radiofrequency power were approximately as above.

TABLE I
SURVIVAL OF AB1157 (WILD TYPE)

Colony scores													
		B treatments											
		1 Control				2 Imaging exposure				3 High field exposure			
A Repeats	1	16	11	13	9	14	19	17	12	13	15	12	15
		14	14	9	10	9	21	12	13	16	15	13	13
		18	8	10	14	14	14	12	14	17	15	16	8
		14	6	12	12	12	17	9	10	14	20	11	10
	2	8	10	12	14	17	15	16	12	12	12	13	16
		13	9	18	7	17	10	14	15	10	12	10	13
		13	12	14	9	17	13	16	10	10	8	15	15
		12	15	5	21	15	12	15	12	10	15	15	14
	3	9	11	15	13	9	16	7	17	20	15	14	20
		14	11	17	18	9	9	11	9	12	9	16	18
		11	10	12	18	11	14	12	9	17	16	21	8
		16	14	16	10	9	13	17	10	12	15	18	12

Two way analysis of variance

Source of variance	Mean squares	Degrees of freedom	F-ratio
Total	10.991	143	
Between cells	25.219	8	
Between repeats (A)	2.583	2	0.2546
Between treatments (B)	24.938	2	2.4573
Interactive (AB)	36.677	4	3.6142*
Within cells	10.148	135	

*Statistically significant.

TABLE II
TUKEY ANALYSIS OF AB1157 SCORES

Comparison of repeats (A) (Averaging over treatments (B))

Cell number	A1	A2	A3
Means	13.1667	12.8750	13.3333

Comparison of cells
A1 × A2 = 0.63
A1 × A3 = −0.36
A2 × A3 = −1.00

Comparison of treatments (B) (Averaging over repeats (A))

Cell number	B1	B2	B3
Means	12.4375	13.0625	13.8750

Comparison of cells
B1 × B2 = −1.36
B1 × B3 = −3.13
B2 × B3 = −1.77

Comparison of individual cells

Means

A\B	1	2	3
1	11.8750	13.6875	13.9375
2	12.0000	14.1250	12.5000
3	13.4375	11.3750	15.1875

Comparison of cells

	A3B3	A2B3	A1B3	A3B2	A2B2	A1B2	A3B1	A2B1
A1B1	−4.16	−0.78	−2.59	0.63	−2.83	−2.28	−1.96	−0.16
A2B1	−4.00	−0.63	−2.43	0.78	−2.67	−2.12	−1.80	
A3B1	−2.20	1.18	−0.63	2.59	−0.86	−0.31		
A1B2	−1.88	1.49	−0.31	2.90	−0.55			
A2B2	−1.33	2.04	0.24	3.45				
A3B2	−4.79*	−1.41	−3.22					
A1B3	−1.57	1.80						
A2B3	−3.37							

*Statistically significant.

TABLE III
SURVIVAL OF MUTANT STRAINS

Colony scores																
B treatments																
		1 Control					2 Imaging exposure					3 High field exposure				
A strains	1 AB2463 *recA*		15	25	20	10		16	22	19	17		13	21	17	22
		24	21	26	14	20	21	16	11	14	22	10	24	20	17	17
		15	21	22	13	17	19	19	18	9	13	17	11	17	13	16
			23	15	28	22		11	16	19	19		21	32	21	16
	2 AB1886 *uvrA*		19	23	16	12		23	16	22	19		22	17	18	11
		18	17	18	27	15	16	19	19	10	15	22	12	9	13	14
		18	22	12	19	16	14	28	11	23	10	23	20	23	25	15
			16	11	12	21		24	17	21	22		17	14	14	12
	3 N2125 *uvrA* *recA*		11	18	12	14		12	9	13	12		11	9	6	13
		10	14	14	17	13	9	15	12	16	10	10	7	13	10	17
		15	10	10	11	9	14	19	9	13	8	10	12	12	16	12
			14	11	7	8		10	9	13	11		11	12	12	14

Two way analysis of variance

Source of variance	Mean squares	Degrees of freedom	F-ratio
Total	25.210	161	
Between cells	171.816	8	
Between strains (A)	639.747	2	36.4639*
Between treatments (B)	11.710	2	0.6674
Interactive (AB)	17.904	4	1.0205
Within cells	17.545	153	

*Statistically significant

TABLE IV
TUKEY ANALYSIS OF MUTANT SCORES

Comparison of strains (A) (Averaging over treatments (B))									
Cell number	A1	A2	A3						
Means	18.0926	17.4444	11.8333						
Comparison of cells	A1 × A2 = 1.14 A1 × A3 = 10.98*	A2 × A3 = 9.84*							
Comparison of treatments (B) (Averaging over strains (A))									
Cell number	B1	B2	B3						
Means	16.3148	15.6296	15.4259						
Comparison of cells	B1 × B2 = 1.20 B1 × B3 = 1.56	B2 × B3 = 0.36							
Comparison of individual cells									
Means	A\B	1	2	3					
	1	19.5000	16.7222	18.0556					
	2	17.3333	18.2778	16.7222					
	3	12.1111	11.8889	11.5000					
Comparison of cells		A3B3	A2B3	A1B3	A3B2	A2B2	A1B2	A3B1	A2B1
	A1B1	8.10*	2.81	1.46	7.71*	1.24	2.81	7.48*	2.19
	A2B1	5.91*	0.62	−0.73	5.51*	−0.96	0.62	5.29*	
	A3B1	0.62	−4.67	−6.02*	0.23	−6.25*	−4.67		
	A1B2	5.29*	0.00	−1.35	4.90*	−1.58			
	A2B2	6.87*	1.58	0.23	6.47*				
	A3B2	0.39	−4.90	−6.25*					
	A1B3	6.64*	1.35						
	A2B3	5.29*							

*Statistically significant.

plate can be treated as a cell and the Tukey method (Veldman, 1967; Youngman, 1975) used to compare cell means. First, we can take the cells in groups of three, averaging over repeats (A) or treatments (B) as shown in the upper part of Table II. The q factors thus obtained are not significant indicating that there is no net difference between repeats or treatments. Second, when we compare each cell with every other cell, as shown in the lower part of Table II, it becomes clear that it is a high mean (increased viability) for cell A3B3 (third repeat of the high field treatment) which is the source of the variance. Since there is no significance of the high field treatment when averaged over repeats (B1 × B3 and B2 × B3) we may conclude that neither it nor NMR imaging adversely affects the viability of the cells under the conditions employed.

2. *Survival of repair deficient strains of* E. coli

As bacteria have mechanisms which act to repair damage to DNA (Witkin, 1976), slight damage may not become apparent through its efficient repair. There are three main pathways through which this can be effected: photoreactivation, recombination and excision repair. Photoreactivation is important only for the repair of UV-induced effects, whereas recombination and excision repair are associated with other types of damage. It is possible to block either or both of these latter pathways in certain bacterial strains, *e.g. recA* (recombination) or *uvrA* (excision). In a strain with both mutations present, the slightest damage to DNA is often lethal (for example 3 J M^{-2} UV reduces the survival of N2125 (see below) by four orders of magnitude whilst leaving the normal strain largely unaffected.) By using strains carrying these mutations it should therefore be possible to see more clearly if any DNA damage is being produced.

Materials and methods. Using the bacteriological methods described above plates were prepared with three different strains, namely, AB2463=*recA*, AB1886=*uvrA* (Bachman, 1972), and N2125, a double *uvrA recA*, derived by crossing AB1886 with KL1699 (Bachman, 1972). Eighteen drops were used for each plate and exposure was for five hours.

Results and analysis. The individual plate scores and a statistical analysis are shown in Table III. The variance suggests that there are real differences between the survival of the different strains, but not between strains exposed to different treatments or to interaction between strains and treatment.

The corresponding Tukey analysis comparing strains (A) averaged over treatments (B) and treatments averaged over strains is shown in the upper part of Table IV. It suggests that although A3, the double mutant, differs from the other two strains it responds equally with respect to the different treatments.

The Tukey analysis in the lower part of Table IV compares each cell with every other cell and shows that cells A3B1, A3B2 and A3B3 differ from all other cells, but not from each other. Thus it is clear that even though N2125 is less viable under control conditions it is as equally unaffected as AB2463 and AB1886 by NMR imaging and high-field exposure.

3. *Reversion*

Changes in the DNA base sequence (mutation) of a structural gene can alter or abolish the function of the gene product. When loss of function prevents synthesis of required metabolites, growth is dependent on supplementation with the appropriate substance. Such a mutant strain can however regain the ability to grow in an unsupplemented medium by reverse mutation (reversion). The frequency of reversion, though very low, can easily be determined by spreading a large number of cells on a medium lacking the growth supplement since only the revertants are able to grow to form colonies. The frequency of reversion is a measure of mutation frequency so that, by scoring colonies, it is possible to determine whether NMR has a mutagenic effect.

Materials and methods. E. coli strain AB1157, which has to be supplemented with biotin, arginine, proline, histidine, threonine and leucine for growth, was used. It was grown in LB to an OD of 0.4 (650 nm) (equivalent to about 2×10^8 cells per ml). The cells were centrifuged, rinsed twice in 56/2 buffer to remove any supplements and finally resuspended in half the initial volume of 56/2 buffer. 0.2 ml of this was evenly spread over the surface of each of 12 agar plates which contained no arginine. These were treated in sets of four for five hours in a high magnetic field of 1 T, during an NMR imaging experiment, and on the laboratory bench as a control. They were then incubated at 37°C for two days before the number of arginine-independent colonies on each plate was counted.

Results. The colony count averages for the high field, imaging and control plates were respectively 14.75, 13 and 17.5. Since these numbers represent the survivors from 10^8 cells, the reversion frequency does not differ significantly between treatments.

4. *Non-mutagenic effects: a bacteriophage induction assay*

The previous experiments indicate that neither NMR nor magnetic fields of up to 1 T cause damage to DNA. However, other forms of damage may occur which would not have been detected in the above assays. Although screening for such general effects is more appropriate in higher organisms, some specific effects can be tested using microbial techniques, for example the function of regulatory proteins and enzymes.

Certain bacterial viruses such as λ have a capacity for stable integration into the bacterial genome. This stable state depends on the production by the integrated virus (prophage) of a repressor protein which prevents those functions which would otherwise lead to multiplication of the virus and lysis of the cell. The inactivation of this repressor leads to production of the phage and cell death. This induction occurs at a low but measurable spontaneous frequency. Cellular damage which affects repressor function should increase the frequency of induction. A strain harbouring λ prophage was therefore exposed to NMR imaging treatment and the frequency of induction was measured by assaying the number of virus particles present.

Materials and methods. Exponential cultures of AB1158 carrying λ prophage KL329 (Bachman, 1972) were grown in LB. Three tubes were exposed to NMR echo-planar imaging for five hours and three, untreated, served as controls.

The number of viable cells and the number of phage particles in each tube were assayed. Cell numbers were assayed in the same manner as described for the AB1157 survival experiments and the number of free virus particles present was determined using standard procedures described by Adams (1959).

Results and analysis. Means were determined for the viable cell and phage assays and a Student's T test used to compare untreated and treated cases. T scores of 1.3817 ($n=24$) and 0.1953 ($n=21$) were obtained for the cell and phage assays respectively, neither of which is significant at the 5% level. Thus echo-planar imaging had no perceivable effect on the induction of λ prophage.

5. *Single enzyme assay*

An analysis was carried out using a bacterial enzyme showing first-order kinetics to see if any effect of a high strength static magnetic field could be detected.

The enzyme used was β-galactosidase which cleaves lactose to produce dextrose and galactose. The reaction is:

ENZYME + SUBSTRATE → ENZYME SUBSTRATE COMPLEX → PRODUCTS + ENZYME

With a saturated enzyme at constant temperature the products accumulate linearly with time.

Materials and methods. *O*-nitrophenyl-β-*D* galactopyranoside (ONPG) was used as substrate and the reaction followed spectrophotometrically by assaying the o-nitrophenol produced.

Reactions were carried out in phosphate buffer (0.06M $Na_2HPO_4.7H_2O$, 0.04M $NaH_2PO_4.4H_2O$, 0.01M KCL and 0.001M $MgSO_4.7H_2O$) at pH 7. For each experiment 50 ml of buffer containing 0.00498M ONPG were placed in a 250 ml flask and the reaction was initiated by addition of 0.25 units of β-galactosidase in 0.1 ml of phosphate buffer. (The enzyme was supplied in 2.2M $(NH_4)_2SO_4$ at pH 6. Each 0.1 ml of this solution contained 250 units of activity; one unit cleaving 1 micromole of ONPG per minute at 37°C.) 2 ml aliquots were removed and placed in 1 ml Na_2CO_3 buffer at pH greater than 11.0 to stop further reaction. The reaction flasks were agitated throughout the experiment and the temperature continually noted.

In the case of the treated flask, the magnet was run for several hours to stabilize the temperature, and the reaction flask was placed in the magnet 15 minutes before time zero to equilibrate. The control was run in a shaking water bath maintained at the same stable temperature as the magnet. The temperature for both was a constant $26° \pm 0.25°C$.

The o-nitrophenol was assayed in a spectrophotometer (UNICAM SP1800 UV) at 420 nm.

Results. The optical densities for the exposed sample and the control agreed to within experimental error at each point in time. We may therefore conclude that the enzyme activity was unaffected by the high field treatment.

CONCLUSION

These experiments show that NMR imaging methods in use in our laboratory do not produce detectable effects in the biological systems studied. As the techniques are very sensitive to low concentrations of toxic chemicals and low doses (cell survival) of UV radiation the absence of any measurable effect after exposure to NMR imaging conditions at field levels in current use suggests freedom from any hazard. The absence of any deleterious effect due to the 1 T magnetic field further suggests that the extension to nuclei other than protons (*e.g.* ^{31}P) will be free from hazard.

ACKNOWLEDGMENTS

We wish to thank the DHSS for support of the NMR imaging project and a post-doctoral fellowship (P.G.M.) and the SRC for a research studentship (A.T.).

We also wish to acknowledge the assistance of other members of the NMR imaging team: Professor P. Mansfield, Professor R. E. Coupland, Dr. I. L. Pykett, Mr. R. Ordidge, Mr. V. Bangert and Mr. R. Rzedzian. Also, Drs. R. G. Lloyd and D. Parkin for their help with strains and statistics respectively.

REFERENCES

Adams, M. H., 1959. *Bacteriophages* (Interscience Publishers Inc., New York).

Ames, B. N., 1971. Detection of chemical mutagens with enteric bacteria. In *Chemical mutagens—principles and methods for their detection*, Ed. A. Hollaender, Vol 2 (Plenum Press, New York), pp. 267–281

Bachman, B. J., 1972. Pedigrees of some mutant strains of Escherichia coli K-12. *Bacteriological Reviews, 36*, 525–557.

Barnothy, M. F., 1964, 1969 (Editor). *Biological effects of magnetic fields*. Vols. 1 and 2 (Plenum Press, New York).

Blakemore, R., Frankel, R. and Wolfe, F., 1979. Magnetite in freshwater magnetotactic bacteria. *Science, 203*, 1355–1356.

Budinger, T. F., 1979. Thresholds for physiological effects due to RF and magnetic fields used in NMR imaging. *IEEE Transactions on Nuclear Science, NS-26*, 2821–2825.

Cooke, P. and Morris, P. G., 1981. The effects of NMR exposure on living organisms II: a genetic study of human lymphocytes. *British Journal of Radiology*, 54, 622–625.

Damadian, R., 1971. Tumour detection by nuclear magnetic resonance. *Science, 171*, 1151–1153

Damadian, R., Goldsmith, M. and Minkoff, L., 1977. NMR in Cancer: XVI. FONAR image of the live human body. *Physiological Chemistry and Physics, 9*, 97–100.

Gadian, D. G., 1977. Nuclear magnetic resonance in living tissue. *Contemporary Physics, 18*, 351–372.

Hinshaw, W. S., Bottomley, P. A. and Holland, G. N., 1977. Radiographic thin-section of the human wrist by nuclear magnetic resonance. *Nature, 270*, 722–723.

Koutcher, J. A., Goldsmith, M. and Damadian, R., 1978. NMR in Cancer X. A malignancy index to discriminate normal and cancerous tissue. *Cancer, 41*, 174–182.

Lauterbur, P. C., 1973. Image formation by induced local interactions: examples employing nuclear magnetic resonance. *Nature, 242*, 190–191.

Low, B., 1973a. Rapid mapping of conditional and auxotropic mutations in *Escherichia coli* K-12. *Journal of Bacteriology, 113*, 798–812.

1973b. Restoration by the rec locus of recombinant forming ability in recB^- and recC^- merozygotes of *Escherichia coli* K-12. *Molecular and General Genetics, 122*, 119–130.

Mallard, J. R., Hutchison, J. M. S., Edelstein, W. A., Ling, C. R., Foster, M. A. and Johnson, G., 1980. *In vivo* NMR imaging in medicine. The Aberdeen approach, both physical and biological. *Philosophical Transactions of the Royal Society, B, 289*, 519–533.

Mansfield, P. and Grannell, P. K., 1973. NMR diffraction in solids? *Journal of Physics, C, 6*, L422–L426.

Mansfield, P., Maudsley, A. A. and Baines, T., 1976. Fast scan proton density imaging by NMR. *Journal of Physics, E, 9*, 271–278.

Mansfield, P. and Pykett, I. L., 1978. Biological and medical imaging by NMR. *Journal of Magnetic Resonance, 29*, 355–373.

Mansfield, P., Pykett, I. L., Morris, P. G. and Coupland, R. E., 1978. Human whole body line-scan imaging by NMR. *British Journal of Radiology, 51*, 921–922.

Mansfield, P., Morris, P. G., Ordidge, R. J., Pykett, I. L., Bangert, V. and Coupland, R. E., 1980. Human whole body imaging and detection of breast tumours by NMR. *Philosophical Transactions of the Royal Society, B, 289*, 503–510.

Moore, W. S. and Holland, G. N., 1980. Experimental considerations in implementing a whole-body multiple sensitive point nuclear magnetic resonance imaging system. *Philosophical Transactions of the Royal Society, B, 289*, 511–518.

Morris, P. G., Mansfield, P., Pykett, I. L., Ordidge, R. J. and Coupland, R. E., 1979. Human whole body line scan imaging by nuclear magnetic resonance. *IEEE Transactions on Nuclear Science, NS-26*, 2817–2820.

Tenforde, T. S., 1978. (Editor). *Proceedings of the Biomagnetics Workshop*. Lawrence Berkeley Laboratory Report No. 7452.

Veldman, D. J., 1967. Fortran programming for the behavioural sciences (Holt, Rinehart and Winston, New York), pp. 257–268.

Witkin, E. M., 1976. Ultraviolet mutagenesis and inducible DNA repair in *Escherichia coli*. *Bacteriological Reviews, 40*, 869–907.

Youngman, M. B., 1975. Programmed methods for multivariate data (University of Nottingham School of Education report).

1981, *British Journal of Radiology*, 54, 622–625

The effects of NMR exposure on living organisms. II. A genetic study of human lymphocytes

By P. Cooke, B.Sc., Ph.D.

Department of Cytogenetics, City Hospital, Hucknall Road, Nottingham NG5 1PB

and *P. G. Morris, M.A., Ph.D.

Department of Physics, University of Nottingham, University Park, Nottingham NG7 2RD

ABSTRACT

The effects of NMR line-scan imaging procedures and static homogeneous magnetic fields of 0.5 and 1.0 tesla on cells from human blood have been investigated by examining their influence on the frequency of gross lesions, sister chromatid exchanges and on the proportion of amodal cells. Cultured human blood cells have also been submitted to extended NMR imaging exposure during active growth and division. Neither treatment had any significant effect on any of the parameters measured.

With the increasing use of NMR techniques for human studies it is of major importance to establish that the procedure has no detrimental physical or genetic effects on the individuals concerned. A brief discussion of potential hazards associated with NMR imaging methods is given in Part I, A microbial assay (Thomas and Morris, 1981).

The present study investigates chromosomal effects both of NMR line-scan imaging and of high static magnetic fields (0.5 and 1.0 T). The latter are of interest since it is likely that NMR studies on humans will extend to nuclei other than protons and these will require higher fields to achieve comparable sensitivity. The details of the NMR imaging experiment are similar to those employed in a recent abdominal scan (Mansfield *et al.*, 1978) and are as described in Part I.

There are at least three ways in which a physical agent could have an adverse genetic effect:

(1) it could increase the rate of point mutation (see Part I);

(2) it could disrupt the genetic material, chromatin, in such a way as to increase the number of sister chromatid exchanges (SCE) or the number of gross chromatid or chromosome lesions (Perry and Evans, 1975);

(3) it could affect the process of cell division, *e.g.* by disrupting spindle formation, thus increasing the risk of obtaining cells with an abnormal number of chromosomes.

With respect to static magnetic field treatment, we have recorded the frequency of SCEs and chromatid and chromosome lesions induced in whole human blood exposed before culture. For the NMR imaging exposure we have assessed the effect on the frequency of SCEs and gross lesions and the proportion of amodal cells in whole blood exposed before culture and in cultured cells exposed during active growth and division.

CULTURE AND SCORING METHODS

All cultures were made up from 0.5 ml of whole blood, 2.5 ml of fetal bovine serum, 7.5 ml of TC 199 and 0.2 ml of phytohaemmaglutanin. In addition, to those cultures on which SCEs were to be scored, 0.1 ml of a 0.5 mg/ml 5-bromo-2′-deoxy uradine (BrdU) solution in physiological saline was added. These cultures were kept in the dark. Harvesting was carried out after incubation at 37°C using a 0.075 M solution of KCl with a 3:1 mixture of

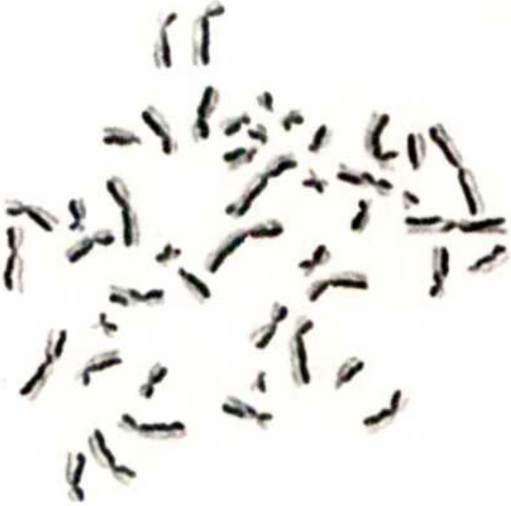


FIG. 1.
Harlequin banding in a cell showing nine SCEs.

---

*Present address and address for reprints: NMR Centre, National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA.

methanol: glacial acetic acid as fixative. Cells were spread on grease-free, ice-cold wet slides and stored for 4–5 days before staining. Cultures scored for chromosome and chromatid breaks were usually harvested after two days and stained with Leishmann, those to be scored for sister chromatid exchange were usually harvested after three days and stained by a modification of the method of Perry and Wolff (1974). A typical result obtained by this procedure is shown in Fig. 1.

The two chromatids of each chromosome stain differentially so that points at which sister chromatid exchange has taken place can be clearly seen. The stained slides were coded by an independent observer to prevent bias.

For the scoring of gross chromosome lesions, either 25 or 100 cells per replicate/individual/treatment were scored whereas for the scoring of the number of amodal cells 50 or 100 cells per replicate/individual/treatment were counted. Sister chromatid exchanges were scored for each individually recognizable pair or group of chromosomes in ten cells from each replicate/individual/treatment. The slides were not decoded until all scoring was completed.

RESULTS

Establishment of appropriate control

Since the material to be treated had to be transported from a different laboratory and would be subject to temperature change in the process of exposure, a preliminary experiment was carried out to make sure that these procedures did not themselves affect the chromosomes. Blood was taken from four individuals and split into two aliquots. One aliquot was kept in the cytogenetics laboratory at room temperature (L), the other aliquot was taken to the physics laboratory and exposed to all circumstances to which the treated material would be subject apart from the treatment itself (T). Four replicate cultures were prepared from each aliquot, two with BrdU for scoring SCE and two without BrdU for scoring chromatid and chromosome gaps and breaks.

There were no significant differences between the two types of control for chromatid lesions ($\bar{x}L = 0.035$; $\bar{x}T = 0.070$. Normal deviate $= 1.53$, non-significant) chromosome lesions ($\bar{x}L = 0.010$; $\bar{x}T = 0.015$. Normal deviate $= < 1$, non-significant), the proportion of cells with lesions (heterogeneity χ^2 (1 df) $= 2.63$, non-significant) or for the mean number of sister chromatid exchanges ($\bar{x}L = 9.56$; $\bar{x}T = 9.99$ VR from analysis of variance for $1/155$ df < 1, non-significant). The control specimens for all subsequent experiments were therefore kept in the laboratory.

Establishment of the validity of two-day harvest for scoring chromatid and chromosome lesions

Chromatid and chromosome lesions should be scored in cells in the first cycle of division after exposure to the agent to be assessed. Recently it has been suggested that a harvest around 48 hours after the initiation of culture could include a relatively high proportion of cells in the second cycle of division (Scott and Lyons, 1979). To check whether this was true in the proposed experiments, cells grown with BrdU were harvested at around 48 hours and the proportion of second cycle cells (*i.e.* those with harlequin banding) scored. Fifty cells were scored from each of four replicates of six individuals grown with and without previous exposure to a 1.0 T static magnetic field.

Heterogeneity χ^2 analysis showed significant differences between individuals in the proportion of second cycle cells present ($\chi^2(5) = 24.74$ $p < 0.5\%$) presumably because of minor variation in their cell-cycle timing or response to transformation but in no case did the proportion of second cycle cells exceed 10%. The presence of no more than 10% of second cycle cells should not distort comparative scoring. Further, this experiment demonstrated that exposure to a high magnetic field did not significantly affect this particular measure of cell turnover ($\chi^2(1) = 0.35$, non-significant).

Exposure to high static magnetic field before culture

Eight samples of blood from six individuals were available. Each sample was split into three aliquots. One aliquot was kept in the laboratory as a control, one was exposed to a static magnetic field of 0.5 T for an hour, the last was exposed to a field of 1 T for an hour. Four replicate cultures were prepared from each aliquot, two with and two without BrdU.

Table I shows the mean scores for each of the parameters measured (the analysis of chromatid and chromosome lesions was performed on only four of

TABLE I

EXPOSURE TO HIGH STATIC MAGNETIC FIELD BEFORE CULTURE. MEAN SCORES PER CELL

Parameter	Treatment		
	Control	0.5 T field	1.0 T field
Chromatid lesions ($\bar{x}$)	0.035	0.015	0.015
Chromosome lesions ($\bar{x}$)	0.010	0.015	0.015
Proportion of cells with lesions	1:22	1:33	1:40
Sister chromatid exchanges ($\bar{v}$)	8.84	9.49	8.88

TABLE II

Exposure to NMR imaging during growth and division. Mean scores per cell

Parameter	2-day		
	Control	Treated	Comparison
Chromatid lesions ($\bar{x}$)	0.018	0.028	1. ND = 1.64 non-sig.
Chromosome lesions ($\bar{x}$)	0.015	0.010	ND = 1.09 non-sig.
Proportion of cells with lesions	1:67	1:56	2. $X^2(1) = 0.64$ non-sig.
Proportion of amodal cells	1:44	1:80	$X^2(1) = 3.49$ non-sig.
	3-day		
	Control	Treated	Comparison
Chromatid lesions ($\bar{x}$)	0.032	0.017	ND = 1.67 non-sig.
Chromosome lesions ($\bar{x}$)	0.013	0.007	ND = 1.14 non-sig.
Proportion of cells with lesions	1:48	1:100	$X^2(1) = 4.71 < 5\%$
Proportion of amodal cells	1:11	1:9	$X^2(1) = 1.58$ non-sig.
Sister chromatid exchanges ($\bar{x}$)	9.32	9.13	3. VR(1/233) = < 1 non-sig.

(1) ND = Normal deviate. (2) X^2 = Heterogeneity χ^2. (3) VR = Variance ratio from analysis of variance.

the eight samples studied). There were no significant differences between treatments for the number of chromatid lesions (normal deviates = control *v.* 0.5 T or 1.0 T = 1.27 non-significant), chromosome lesions (normal deviate = control *v.* 0.5 T or 1.0 T = < 1 non-significant), the proportion of cells with lesions (heterogeneity $\chi^2(2) = 1.34$ non-significant) or the number of sister chromatid exchanges (variance ratios between treatments from analysis of variance for 1/470 df = 1.95 non-significant).

Exposure to NMR imaging before culture

Blood was taken from four individuals and split into two aliquots. One aliquot was kept in the laboratory (C) and the other exposed to a run-up and adjustment period of static magnetic field for 30–50 minutes and a scanning period of 40 minutes. This is the procedure that would normally be used for line-scan NMR imaging. During the procedure the temperature around the exposed blood samples rose by an average of 3.5°C. Four replicate cultures were prepared from each aliquot, two with and two without BrdU.

No significant response to the full imaging procedure (F) was detected in the number of chromatid lesions present ($\bar{x}$C = 0.035; $\bar{x}$F = 0.010. Normal deviate = 1.33 non-significant); chromosome lesions present ($\bar{x}$C = 0.010; $\bar{x}$F = 0.035. Normal deviate = 1.33 non-significant); the proportion of cells with lesions (C = 1:22; F = 1:22; heterogeneity $\chi^2(1) = 0.00$ = non-significant); or the number of sister chromatid exchanges present ($\bar{x}$C = 9.56; $\bar{x}$F = 8.74 variance ratio from analysis of variance for 1/155 df = 2.62 non-significant).

Exposure to NMR imaging during growth and division

Eight blood cultures were prepared from each of six individuals, four with and four without BrdU. All cultures were incubated for 44 hours. Those which were to be harvested after two days then had colcemid added to them. Two cultures from each individual/treatment were kept in the laboratory as controls and two were exposed to the full process for eight hours, the temperature being maintained at 37°C. The two-day cultures were then harvested while those containing BrdU were returned to the incubator for a further 18 hours, colcemid was added and they were harvested six hours later. From the proportion of second-cycle cells present in the two-day harvests of culture treated in this way, exposure over this time period should ensure that a reasonable proportion of cells are somewhere in the late S or G2 of the first cycle, in division or in the early stages of G1 on the second cycle during exposure. The effects of the treatment could be immediately manifest as an increased frequency of lesions in the two-day harvests or have a deferred effect on the three-day harvest, by disruption of segregation and subsequent production of amodal cells or by the production of lesions or SCEs revealed after passage through synthesis of the second cycle.

Table II gives a summary of data collected by scoring the number of chromatid and chromosome lesions, the proportion of cells with lesions and the proportion of amodal cells present in the two- and three-day harvests, together with the results of the sister chromatid exchange data from the three-day harvests and a summary of the statistical comparisons made. Full details of the complete analysis of these and other data presented in this paper can be obtained from the senior author on request. In only one case was a significant difference between control and exposed material obtained. In the three-day harvests the control set had a significantly higher proportion of cells with lesions than the exposed set. No other measured parameter shows any significant difference between the control and exposed material.

Conclusion

This study has demonstrated that a single exposure to NMR line-scan imaging or homogeneous magnetic fields up to 1 T has no significant adverse chromosomal effects on human blood cells. It therefore suggests that NMR imaging as presently employed is free from genetic hazard. The effects of repeated peripheral exposure can be gauged by a similar analysis of blood samples from operatives who are so exposed and we hope to report on this in a subsequent publication.

Acknowledgments

We wish to thank the DHSS for the support of the NMR imaging project and for a post doctoral fellowship (P.M.G.).

REFERENCES

Mansfield, P., Pykett, I. L., Morris, P. G. and Coupland, R. E., 1978. Human whole body line-scan imaging by NMR. *British Journal of Radiology*, *51*, 921–922.

Perry, P. and Evans, H. J., 1975. Cytological detection of mutagen–carcinogen exposure by sister chromatid exchange. *Nature*, *258*, 121–125.

Perry, P. and Wolff, S., 1974. New giemsa method for the differential staining of chromatids. *Nature*, *251*, 156–158.

Scott, D. and Lyons, C. Y., 1979. Homogeneous sensitivity of human peripheral blood lymphocytes to radiation induced chromosome damage. *Nature*, *278*, 756–758.

Thomas, A. and Morris, P. G., 1981. The effects of NMR exposure in living organisms. I. A microbial assay. *British Journal of Radiology*, *54*, 615–621.

Book reviews

Known Effects of Low-Level Radiation Exposure—Health Implications of the Three Mile Island Accident (April, 1979). 47 pp. 1980. NIH Publication No. 80-2087, (US Dept. of Health, Education and Welfare, Washington, D.C.).

This publication is the proceedings of a conference convened in Pittsburgh, Pa., on April 25, 1979 to inform local physicians and public health officials on the known effects of low-level radiation exposures, in the immediate aftermath of the TMI accident. The interval of only one month between the accident and the conference was obviously too short for a thorough evaluation of all the data, and the reports given by the various experts from universities and from the national laboratories were designed primarily to allay the excessive fears aroused by the many confused accounts which had issued from the authorities, the utilities and the media during the preceding weeks. The talks and discussion have been reproduced verbatim, presumably from tapes, and this certainly conveys some of the tension in the conference. While the formal presentations are, in general, quite clear and may be considered as reassuring, the verbatim reports of the question and answer sessions which followed the talks are far from clear and are liable to raise many doubts again. Dr. Sternglass was the most persistent questioner and he did not always receive satisfactory on-the-spot answers. It would surely have been better to have dealt fully with all such questions in the published report, as was done in the particular case of iodine uptake, where Dr. Brodsky's considered statement does indeed clarify the situation and allay concern on this point. This is not the document to which one would turn, however, for a complete or final analysis of the Three Mile Island accident.

J. W. Boag.

Introduzione alla Medicina Nucleare. By Luigi L. Barbieri, pp. 152, 1980. (Patron, Bologna), L. 1200.

If anyone buys this book in the hope of learning about nuclear medicine, he will be disappointed. The subject matter is the physics of radioactivity, interactions of ionizing radiation with matter and an introduction to the biological effects of radiation. The text is simple and clearly set out and would be a good introduction to the scientific basis of the uses of radioactivity in medicine. My only caveat is in the chapter on biological effects of raditions where no distinction is drawn between RBE and QF; indeed they are stated to be identical. It is also strange, in a book published in 1980, to find no mention of the SI units of radiation and radioactivity.

D. K. Bewley.

1981, *British Journal of Radiology*, *54*, 626–629

The iodine concentration in benign and malignant thyroid nodules measured by X-ray fluorescence

By *T. G. Tadros, Ph.D., M. N. Maisey, B.Sc., M.D., F.R.C.P.,
S. C. Ng Tang Fui, M.Sc., M.B., B.S., M.R.C.P. and P. C. Turner, M.Sc.

Departments of Nuclear Medicine and Endocrinology, Guy's Hospital, London SE1 9RT

(*Received August 1980 and in revised form January 1981*)

ABSTRACT

Iodine concentration was measured by X-ray fluorescence in 48 normal thyroid glands obtained at autopsy and in 91 surgical thyroid specimens with a variety of abnormalities. The iodine concentration in normal thyroids ranged from 0.02 to 3.12 mg/g of tissue with a mean value of 1.03 ± 0.67 mg/g. The concentrations in pathological specimens were generally lower with the lowest values found in thyroid cancers. Sixteen (76%) of 21 malignant thyroid specimens analysed had undetectable iodine (<0.02 mg/g) whereas 22 (96%) of 23 benign nodules had measurable iodine concentrations. The detection of iodine in a thyroid nodule by X-ray fluorescence pre-operatively would significantly decrease the probability of malignancy and the need for surgical excision.

Until recently, *in vivo* investigation of the thyroid has been exclusively dependent on the systemic administration of radionuclides such as radioactive iodine or ^{99}Tc^{m} which are concentrated by the thyroid (Ng Tang Fui and Maisey, 1979). However, studies with radioiodine tracers reflect the metabolic turnover, *i.e.*, the rate of uptake or release of iodine by the thyroid, but do not provide an accurate assessment of total iodine content of the gland (Robertson *et al.*, 1976).

Over the past few years, a new technique based on the principle of X-ray fluorescence (Hoffer *et al.*, 1971; Patton *et al.*, 1976) has been developed for investigating the thyroid without introducing any radionuclides into the body. Intrathyroidal stable iodine (^{127}I) is activated *in situ* by an external source of γ rays directed towards the neck, resulting in the release of characteristic fluorescent X rays which can be measured with a suitable detector. The fluorescent technique has been applied mainly to scanning systems to image the thyroid according to the regional distribution of stable iodine in the gland. The main advantage of the technique lies in the very low radiation dose to the patient's neck without any exposure to the rest of the body (Hoffer *et al.*, 1971).

The diagnostic usefulness of the fluorescent scan depends on the demonstration of a correlation between the iodine content or concentration of the thyroid and specific disease processes. The technique has attracted special attention as a possible means of diagnosing thyroid cancer (Patton *et al.*, 1976). Hoffer (1969) originally postulated that malignant thyroid nodules, which as a rule cannot be distinguished from benign solitary cold nodules on the conventional radionuclide scan owing to their poor radionuclide uptake, might synthesize and store significant amounts of iodoproteins and thus be differentiated by their ^{127}I content with the fluorescent scan. However, their assumption was not confirmed when they subsequently reported (Hoffer *et al.*, 1971) that thyroid nodules with poor radioiodine uptake all had very low content of stable iodine irrespective of their benign or malignant nature. However their fluorescent technique did not include quantitative assessment of the ^{127}I content of the nodules.

Subsequently, Patton *et al.* (1976) investigated the problem quantitatively by means of an *in vivo* computerized fluorescent scanning system to determine the ratio of stable iodine in solitary thyroid nodules to that of the opposite normal lobe. They reported that the iodine content ratio for malignant nodules (less than 0.6) was significantly lower than that of benign nodules (over 0.6) and claimed that their technique could differentiate benign and malignant nodules with an accuracy of 90%. However, their findings have not yet been confirmed.

The purpose of the present study was to investigate with an *in vitro* fluorescent technique the stable iodine concentration of surgically removed thyroid tissues with particular reference to benign and malignant nodules, in order to assess the possible value of *in vivo* X-ray fluorescence in the preoperative diagnosis of solitary thyroid nodules.

MATERIALS AND METHODS

The material examined consisted of 48 normal thyroids obtained at autopsy from patients with no history of thyroid disease and 91 surgical specimens from patients with a variety of thyroid diseases who underwent thyroidectomy. Twenty-one of the surgical specimens were malignant, of which 16 were differentiated follicular or papillary carcinomas, one

---

Address for reprints: Dr. M. N. Maisey, Department of Nuclear Medicine, Guy's Hospital, London SE1 9RT.

*Present address: Kasr El-Einy Centre of Radiation, Cairo University Faculty of Medicine, Egypt.

anaplastic and two medullary carcinomas and two were malignant thyroid lymphomas. The remaining surgical specimens were histologically diagnosed to be benign adenomas or colloid nodules (23), Hashimoto's thyroiditis (10), simple multinodular goitre (15) and toxic goitres (22).

From each autopsy or surgical specimen, five pieces were taken from different sites, weighed individually and dissolved in an equal volume of molar sodium hydroxide solution by incubation at 80°C resulting in a two-fold dilution of iodine concentration. The benign and malignant nodules were carefully dissected out from the paranodular tissue before iodine measurement. One millilitre of each dissolved thyroid specimen was used for measurement of iodine concentration and distilled water was counted for background correction. A calibration curve was constructed from measurement of serial dilution of a standard solution of potassium iodide.

Iodine concentration was measured by X-ray fluoresence using an *in vitro* method similar to that described by Moss *et al.* (1972). The method is illustrated in Fig. 1. Each sample was placed in a disposable cuvette and irradiated by a collimated beam of 59.5 keV γ rays from an 11 GBq (300 mC) sealed source of ^{241}Am (Radiochemical Centre Ltd.). The emitted radiation was detected by a collimated 80 mm^2 silicon (lithium-drifted) semi-conductor detector (Kevex Corporation) with its axis perpendicular to the irradiating beam and linked to a multi-channel analyser (ND 100). The observed energy spectrum of the emitted radiation (Fig. 2) showed peaks due to the characteristic fluorescent X rays of iodine and Compton scattering of the incident ^{241}Am γ rays. The number of counts in the iodine Kα peak was recorded after counting each sample for 40000 counts in a narrow region of the Compton scatter peak (Tadros, 1978). The background count was subtracted and the concentration of iodine in the irradiated sample was derived from the calibration curve.

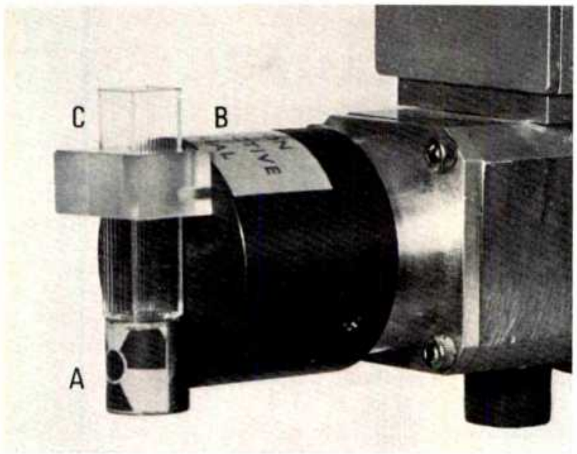


FIG. 1.

X-ray fluorescent technique: close-up of source, sample and detector. A, ^{241}Am source. B, anterior end of detector. C, cuvette for sample.

RESULTS

Figure 3 shows the calibration curve that was obtained from irradiation of the various standard potassium iodide solutions. The iodine concentration corresponding to the counts in the Kα peak for the normal and pathological thyroid specimens were derived from the calibration curve and have been plotted in Fig. 4. Each value represents the mean iodine concentration for the five pieces of tissue obtained from each specimen. Using a 99% confidence limit, the lowest iodine concentration detectable by this technique was 0.01 mg per ml of solution in the cuvette or 0.02 mg per g of thyroid tissue.

DISCUSSION

Our results indicate a mean iodine concentration of 1.03±0.67 mg/g of tissue (range 0.02–3.12 mg/g) in normal thyroids. This is not significantly different from the mean normal level of 0.98 mg/g reported by Le Blanc *et al.* (1973) in Texas using an X-ray fluorescent technique. Fisher and Oddie (1969) using chemical methods found a mean total iodine content of 15 mg in normal fresh cadaver thyroids with average weight of 14.54 g, *i.e.*, a mean iodine concentration (1.03 mg/g) similar to the value we obtained. Comparable values were observed from *in vivo* radioidodine clearance studies by the same investigators. These values however are significantly

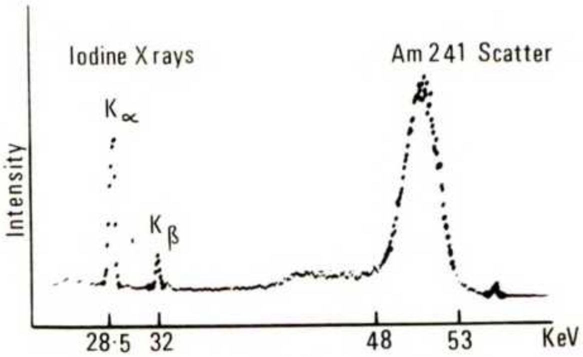


FIG. 2.

Energy spectrum of photons produced during irradiation of sample containing iodine.

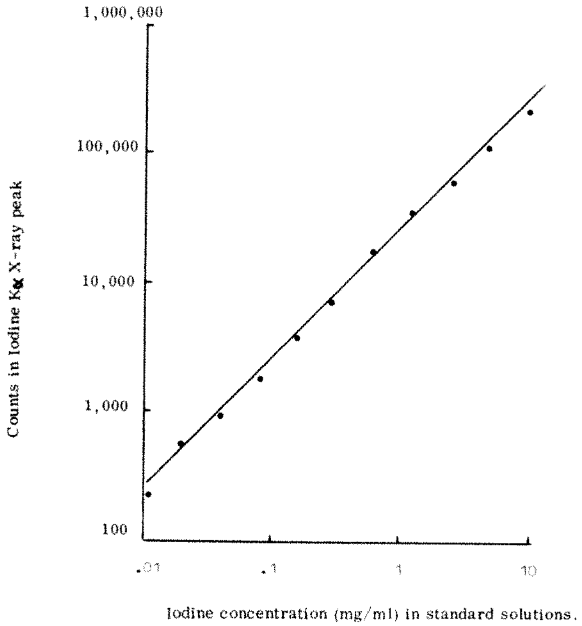


Fig. 3.

Calibration curve of iodine in KI solutions.

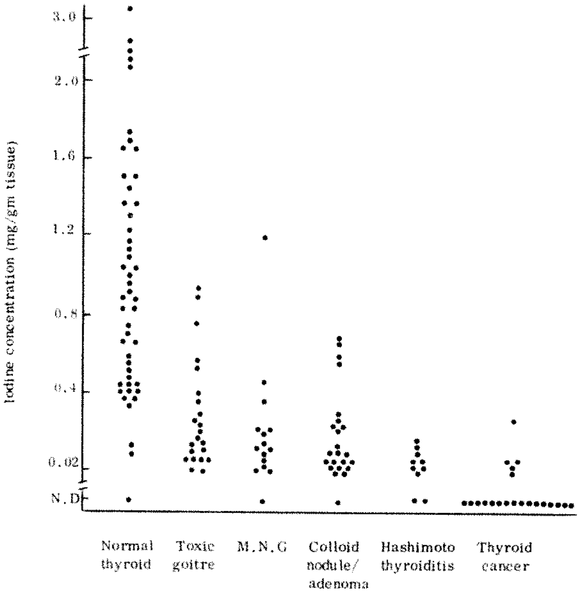


FIG. 4.

Iodine concentration in normal and pathological thyroid tissue. ND, not detectable. MNG, multi-nodular goitre.

higher than those observed in various countries by earlier investigators using different techniques as reported by Hellstern *et al.* (1978) and may represent a true increase in normal thyroid iodine content associated with the modern increase in iodine intake (Le Blanc *et al.*, 1973) rather than the different methodology of iodine measurement. A fall in radioiodine uptake by the normal thyroid in recent years has also been related to the increase in dietary ingestion of iodine (De Groot and Stanbury, 1975).

Statistical analysis of our data showed no significant variation in the normal thyroidal iodine concentration with sex or age (25–80 years). The majority of normal thyroids we analysed had iodine concentrations in the range 0.3 to 3.1 mg/g; this degree of variation has also been noted by other investigators (Fisher and Oddie, 1969). However, three apparently normal thyroids we analysed had very low iodine concentrations (less than 0.3 mg/g) the cause of which is unknown.

The mean iodine concentration for each pathological tissue type was significantly lower than the mean normal value but there was some degree of overlap between the ranges of values for each histological group. Thus iodine concentration was not significantly different in toxic goitres, simple multinodular goitres and solitary benign nodules. This contrasts with the difference in radioiodine uptake usually seen in these conditions—high in diffuse toxic goitres and low in benign non-functioning nodules—indicating that iodine storage in the thyroid is not directly related to its iodine uptake as previously noted by Thrall *et al.* (1977). It has been reported (Jonckheer and Deconinck, 1979) that the total iodine content of diffuse toxic goitres may be higher than that of normal thyroids; our findings would indicate that this is due mainly to the larger mass of toxic goitres rather than their iodine concentration which was often normal or subnormal in our series.

The lowest iodine concentration in the present study was found in thyroid cancer. Sixteen (76%) of the 21 malignant specimens examined had undetectable iodine (< 0.02 mg/g); in two of them, iodine concentration was only just detectable while the remaining three specimens had concentrations only slightly above the lowest detectable value. These three malignant thyroid tumours included one micro-angio-invasive follicular carcinoma and one papillary carcinoma, each containing numerous colloid-filled follicles, and one medullary carcinoma with invaded residual normal follicular thyroid tissue. The low iodine concentration in anaplastic thyroid cancer and in thyroid lymphomas is attributable to the lack of thyroid follicles in these tumours. In the case of papillary or follicular carcinomas, although thyroid follicles are usually present, their endocrine function, *e.g.*, iodine uptake, is usually very low at the time of diagnosis although it often improves after thyroid ablation under high serum TSH stimulation (Edmunds *et al.*, 1977).

Compared with the high proportion of malignant nodules with undetectable iodine, 22 (96%) of the 23 benign nodules we examined had measurable iodine concentrations, ranging from 0.02 to 0.68 mg/g of tissue, indicating that benign nodules are able to store iodine more efficiently than the malignant tumours although less efficiently than normal thyroid tissues. We have also analysed the fluid aspirated percutaneously from three simple thyroid cysts following ultrasound investigation and found no detectable iodine in any of them. However, although thyroid cysts appear as cold nodules on radionuclide scan, they can now be diagnosed accurately by ultrasound examination and rarely constitute a diagnostic problem with regard to malignancy (Ng Tang Fui and Maisey, 1979). The *in vivo* detection of stable iodine in a thyroid nodule by X-ray fluorescence would thus significantly decrease the probability of malignancy assuming that the sensitivity of the detecting system is sufficiently good to detect iodine concentrations of the order of 0.02 mg/g. Conversely, the absence of detectable iodine stores in a solid nodule would increase the probability of malignancy. As current non-invasive methods of distinguishing between benign and malignant thyroid nodules are only of limited value, the *in vivo* fluorescent technique would contribute significantly to the pre-operative assessment of nodular goitres and help the clinician in selecting those nodules that require surgical excision. Solitary thyroid nodules which are cold on radionuclide scan, solid on ultrasound examination and devoid of iodine on X-ray fluorescent study, should always be excised as they carry the highest risk of malignancy. A study of the *in vivo* application of other X-ray fluorescence techniques in the assessment of solitary thyroid nodules is in progress.

ACKNOWLEDGMENTS

T. G. Tadros was supported by the Arab Republic of Egypt Educational Bureau, London, and S. C. Ng Tang Fui was in receipt of a research grant from the Guy's Hospital Special Trustees. This work was also supported in part through a grant from the *Sunday People* newspaper, Man of the People Fund.

REFERENCES

DE GROOT, L. J. and STANBURY, J. B., 1975. In *The Thyroid and its Diseases.* 4th Edit. (John Wiley, New York), pp. 122–123.

EDMONDS, C. J., HAYES, S., KERMODE, J. C. and THOMPSON, B. C., 1977. Measurement of serum TSH and thyroid hormones in the management of treatment of thyroid carcinoma with radioiodine. *British Journal of Radiology, 50,* 799–807.

FISHER, D. A. and ODDIE, T. H., 1969. Thyroid iodine content and turnover in euthyroid subjects. Validity of estimation of thyroid iodine accumulation from short term clearance studies. *Journal of Clinical Endocrinology, 29,* 721–727.

HELLSTERN, P., KELLER, H. E., WEINHEIMER, B. and WESCH, H., 1978. Thyroid iodine concentration and total thyroid iodine in normal subjects and in endemic goitre subjects. *Clinical Endocrinology, 9,* 351–356.

HOFFER, P. B., 1969. Fluorescent thyroid scanning. *American Journal of Roentgenology, 105,* 721–727.

HOFFER, P. B., BERNSTEIN, J. and GOTTSCHALK, A., 1971. Fluorescent techniques in thyroid imaging. *Seminars in Nuclear Medicine,* 1, 379–389.

JONCKHEER, M. and DECONINCK, F., 1979. Dissociation between iodine storage function and hormone function as observed with XRF scanning of the thyroid. Paper at *10th Annual meeting of the European Thyroid Association.* Abstract in *Annales d'Endocrinologie* , vol. 40.

LE BLANC, A. D., BELL, R. L. and JOHNSON, P. C., 1973. Measurement of ^{127}I concentration in thyroid tissue by X-ray fluorescence. *Journal of Nuclear Medicine, 14,* 816–819.

MOSS, A. A., KAUFMANN, L. and NELSON, J. A., 1972. Fluorescent excitation analysis: a simplified method of iodine determination *in vitro. Investigative Radiology, 7,* 335–338.

NG TANG FUI, S. C. and MAISEY, M. N., 1979. Radio nuclide thyroid scanning. *Hospital Update, 5,* 209–227.

PATTON, J. A., HOLLIFIELD, J. W., BRILL, A. B., LEE, G. S. and PATTON, D. D., 1976. Differentiation between malignant and benign solitary thyroid nodules by fluorescent scanning. *Journal of Nuclear Medicine, 17,* 17–21.

ROBERTSON, K., BODDY, K., HOOPER, M. J., STEVENSON, R. D., MCGHIE, T., ALEXANDER, W. D. and WILSON, G. M., 1976. Total thyroidal content of iodine in thyrotoxic patients measured by *in vivo* neutron activation analysis. *Clinical Endocrinology, 5,* 151–157.

TADROS, T. G., 1978. Fluorescent excitation analysis in clinical and endocrinological investigations (Ph.D. thesis, University of London).

THRALL, J. M., BURMAN, K. D., GILLIM, M. T., CORCORAN, R. J., JOHNSON, M. C. and WARTOFSKY, Z., 1977. Solitary autonomous thyroid nodules: comparison of fluorescent and pertechnetate imaging. *Journal of Nuclear Medicine,* 18, 1064–1068.

1981, *British Journal of Radiology*, *54*, 630–631

Technical note

A water bath for thyroid scanning with ultrasound

By L. A. Berger, F.R.A.C.P., F.R.C.R., A. Lister, B.Sc. and A. C. Lilley

Department of Diagnostic Radiology and Inter-Departmental Mechanical Work-Shop, The Royal Free Hospital, Pond Street, London NW3 2QG

(*Received October 1980 and in revised form January 1981*)

Ultrasound examinations of the thyroid and parathyroid glands are becoming more frequent. Although contact scanning is still preferred by some, most ultrasonographers employ a water bath. The conventional water bath consists of a metal frame with a plastic or polythene sheet. This costs £368 and is somewhat cumbersome to use. The unit described below is very light, inexpensive and easy to use. Furthermore, the design could be modified to make a purpose-built water bath for use elsewhere.

Description

The shape of the water bath can be seen from Fig. 1. Details of the construction are illustrated in Fig. 2. The tank is constructed from a moulded Cabulite sheet 2 mm (0.08 inch) thick. This is drawn down over a mould on a vacuum-moulding machine. The excess material is trimmed off and the base cut out with a sharp knife leaving a lip. A sheet of 0.38 mm (0.015 inch) silicone rubber is glued to the lip using cyanoacrylate adhesive (Super-Glue). Any excess rubber is removed.

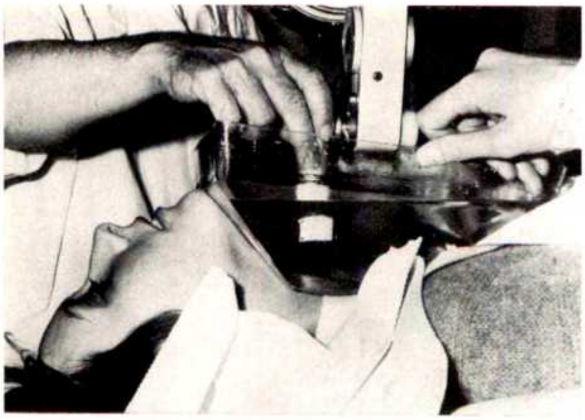


FIG. 1.

The water bath in use. Note that the bath is supported by the patient's shoulders and neck and that she is lightly steadying it with her hands. Paper protects the patient's hair from the oil.

The mould itself is made from wood which has been filled, smoothed and polished. Alternatively, the mould can be made from polystyrene. This is cut to shape using a hot wire and hardboard profiles are placed on either side of the polystyrene block to act as guides. The polystyrene is then coated with plaster of paris and is smoothed and shaped by hand. This type of mould is inexpensive but does tend to crack and does not last very long.

Method of use

The patient lies supine with a pillow beneath the shoulders and the head hyper-extended. Both the

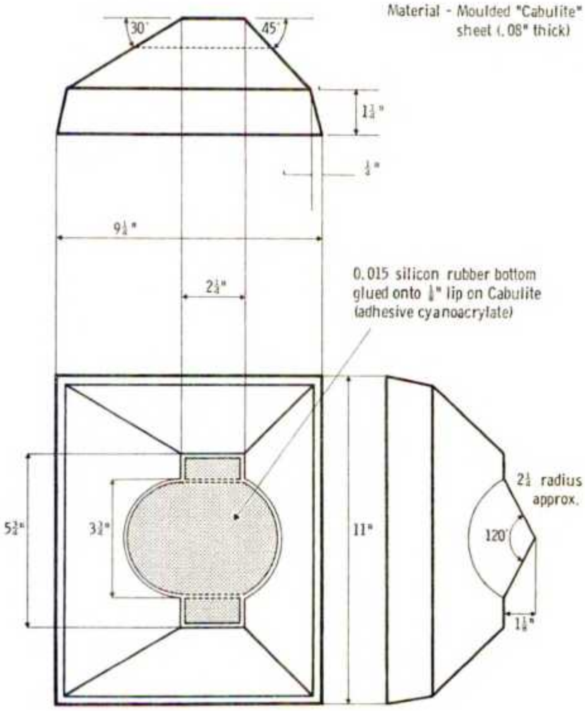

Material - Moulded "Cabulite" sheet (.08" thick)
30°
45°
1¼"
¼"
9¼"
2¼"
0.015 silicon rubber bottom glued onto ⅛" lip on Cabulite (adhesive cyanoacrylate)
5¾"
3¼"
11"
2¼ radius approx.
120°
1¼"

Fig. 2.

Diagram to illustrate details of the water bath. Dimensions are in inches (25.4 mm).

patient's neck and silicone rubber are coated with oil and the unit is then placed on the patient's neck and shoulders. The unit is so designed that most of the weight is borne by the shoulders. The bath is then filled with water at body temperature to the required depth and scanning performed (Fig. 1).

The bath will balance easily on the patient's shoulder and neck but as a safeguard we usually ask the patient to steady the bath with the hands.

The use of this bath results in high-class scans achieved with minimum of effort and discomfort for the patient. We have only encountered one patient who, because of a very stiff neck, could not be scanned using this water bath.

Book review

Investigative Ultrasonology. 1. Technical Advances. Ed. by C. R. Hill and C. Alvisi, pp. ix+165, 1980 (Pitman Medical, Tunbridge Wells), £14·95.
ISBN 0-272-79575-5

This well-produced volume comprises the proceedings of three workshops and a review lecture which constituted part of the Third European Congress on Ultrasonics in Medicine, held at Bologna in 1978. There are some 30 contributions, divided into sections (one per workshop): automatic and computer-aided sonography (nine papers); living tissue identification and movement analysis (nine papers); and dosimetry control of ultrasound and standardization of equipment (seven papers). A useful feature of the text is the inclusion of the salient points of the discussions which took place. For the second section these are collectively summarized, while for the last section the summary is included at the end of each of the papers that were presented. The topics and contributors appear to have been selected by the workshop chairman with the result that each workshop presents a mixture of summarized new developments and superficial reviews.

The first section includes descriptions of computing systems applied to mechanically and electronically scanned imaging systems to permit manipulation of the displayed image with particular reference to obstetrics, breast disease, and prostate tumours. There are four excellent reviews of signal analysis in ophthalmology, ultrasonic computer-assisted tomography, and digital techniques in Doppler investigations and M-scan interpretation. Two final papers, on the possibility of performing image processing in real-time of moving organs, consider digital and optical techniques respectively. A large fraction of the material in this section is speculative. The value of what is not speculative, with a few exceptions, is masked behind the two stages from a technological advance to a significant development, namely whether the advances reported can be developed into commercial instruments, and whether these will prove to have an important place in the range of diagnostic aids available.

The second section, on living tissue identification and movement analysis, was, the introduction states, intended as a dialogue between the clinical "users" and the scientific engineering "providers" of methods of tissue characterization. The contributions vary in length between one and five pages, many of them being only two or three pages long. Curiously there are no photographs at all in this section, and only one paper (the editor's) contains diagrams. The first four contributions point to the problems and high hopes and expectations of clinical specialists in internal medicine, gynaecology and breast disease, cardiology and ophthalmology. The answer from the scientists was equally optimistic, the degree of optimism expressed being in inverse relation to the extent of the feasibility studies reported, and the explicit recognition of the problems involved. The techniques discussed were diffraction analysis, multi-frequency analysis, reconstruction of interaction coefficients (an excellent review), Doppler flow analysis, and tissue and organ dynamics analysis. This last paper featured often in the discussion which concluded with stress on the development of techniques which are simple and inexpensive.

The final section on "dosimetry" and the standardization of equipment contains, without exception, informative review articles. They deal with the biophysical basis of "dosimetry", methods of measuring exposure including potential *in vivo* techniques, the UK national standards development, system performance measurements, the status of ultrasound diagnostic imaging standards in the USA, and the work and responsibilities of International Agencies. Although a considerable amount of detail is absent from these papers they collectively represent a useful entry to the topic.

In summary, this well-indexed book includes a considerable amount of clinically relevant technical material and speculation. It is likely to be of particular value to those wishing to start investigation of a particular technical approach. The delay in its production and the speed of developments in medical ultrasound may reduce its long-term value.

R. C. CHIVERS.

1981, *British Journal of Radiology*, *54*, 632

Case reports

Vocal-cord paralysis after treatment of thyrotoxicosis with radioiodine

By A. M. Robson, M.B., B.Ch., B.A.O.

Department of Radiotherapy, Coventry and Warwickshire Hospital, Coventry CV1 4FH

(*Received November 1980*)

Experience has shown that radioiodine (^{131}I) is a convenient and safe method of treatment for thyrotoxicosis. Injury to the recurrent laryngeal nerve causing vocal-cord paralysis is an unexpected complication of this treatment, but a recognized hazard of thyroid surgery (*Lancet*, 1970). This is the first report of vocal-cord paralysis occurring in the United Kingdom after radioiodine treatment for thyrotoxicosis.

Case Report

A 65-year-old retired accountant presented in December 1977 with loss of weight of about 11 kg over the previous 15 months, coinciding with a period of domestic stress, and a four-month history of tremor, loss of energy and wasting of the proximal muscles of his arms and legs. On examination he had classical signs of thyrotoxicosis without exophthalmos. The thyroid did not appear clinically enlarged.

Investigations showed a total serum thyroxine of 196 n mol/l (normal range 45–160 n mol/l) and positive fluorescent thyroid antibodies. Haematology, biochemistry, ECG and chest radiograph were normal.

He was treated initially with carbimazole for 15 weeks. After an interval of 12 days he was given 222 MBq (6 mCi) of radioiodine (^{131}I) and carbimazole was recommenced three days afterwards. On the next day he presented with hoarseness which had suddenly developed two days after he had received the radioiodine. Indirect laryngoscopy showed a complete right vocal-cord paralysis. A tomogram of the thoracic inlet and a repeat chest radiograph were normal. His voice returned to normal four months after the radioiodine had been given, but complete paralysis of the cord remained on laryngoscopy for a further four months. Some return of function was then seen and by the 15th month after radioiodine administration almost full recovery had taken place. Carbimazole was finally discontinued four months later, after two years and three months of treatment. To date there has been no sign of relapse.

Discussion

Vocal-cord paralysis after radioiodine has been reported only twice (Craswell, 1972; Snyder, 1978), but never from the United Kingdom, where some 3000 patients are treated annually (Tubiana, 1971).

^{131}I emits mainly β-particles which penetrate a few millimetres only into surrounding tissues and so do not harm anatomically-related structures (Greene, 1980). Why then should injury to the recurrent laryngeal nerve have occurred, considering that ablation dosages of ^{131}I given for thyroid carcinoma—without expectation of vocal-cord paralysis as a sequel—are some 20 times those given for thyrotoxicosis?

Certainly local swelling of the thyroid is a transient, but usually mild, feature of radioiodine treatment and is thought to be caused either by a radiation thyroiditis or an increased thyroid metabolic activity due to the temporary withdrawal of antithyroid drugs (Havard, 1974). Rarely corticosteroids must be given for its control.

The rapidity of onset of paralysis of the vocal cord in this case suggests that the injury to the recurrent laryngeal nerve was not radiation-induced but more likely a result of pressure on the nerve from either transient swelling in an adenomatous nodule in the gland adjacent to the recurrent laryngeal nerve, as has been suggested by Craswell (1972), or transient diffuse swelling of the thyroid compressing the nerve, possibly against a tracheal cartilage or because of some other individual anatomical characteristic, when it lies in close relation to the posterior surface of the gland.

Complete recovery in this case took 15 months, whereas in some surgical cases this occurs in a shorter time (*Lancet*, 1970). It is, of course, not proven that this was a complication of the radioiodine treatment, but it is felt to be noteworthy. If it was related to the radioiodine it must be a very rare complication.

Acknowledgments

I wish to thank Dr. T. W. Backhouse for encouragement and advice, and Dr. K. D. Lee for permission to publish this case.

REFERENCES

Craswell, P. W. T., 1972. Vocal cord paresis following radioactive iodine therapy. *British Journal of Clinical Practice*, *26*, 571–572.

Greene, R., 1980. Treatment of thyrotoxicosis. *Prescribers' Journal*, *20*, 73–80.

Havard, C. W. H., 1974. The management of thyrotoxicosis. *British Journal of Hospital Medicine*, *11*, 893–908.

Lancet, 1970. Editorial, The recurrent laryngeal nerve at thyroidectomy. *Lancet*, *i*, 398.

Snyder, S., 1978. Vocal cord paralysis after radioiodine therapy. *Journal of Nuclear Medicine*, *19*, 975–976.

Tubiana, M., 1971. Therapeutic use of radioactive isotopes. In *Radioisotopes in Medical Diagnosis*, Ed. E. H. Belcher and H. Vetter (Butterworths, London), pp. 751–767.

1981, *British Journal of Radiology*, *54*, 633–635 JULY 1981

Case reports

Antenatal diagnosis of duodenal atresia

By *P. Farrant, D.C.R.M.U., †K. C. Dewbury, B.Sc., M.B., B.S., F.R.C.R. and
*H. B. Meire, M.B., B.S., F.R.C.R.

*Division of Radiology, Clinical Research Centre, Harrow HA1 3UJ and †Radiology Department, Southampton General Hospital

(*Received November 1980*)

The detection of duodenal atresia *in utero* has been previously reported. We report two further cases in which a definitive diagnosis was possible due to oblique scans showing the connection between the fluid-filled stomach and duodenum.

The incidence of duodenal atresia is reported as one in 6000 births (Irving and Rickham, 1978) Hydramnios was present in 53% of cases. Fonkalsrud *et al.* (1969), in a review of 503 cases, reported that associated malformations were present in 48% of cases. The most common associated malformation was Down's syndrome, which was present in 33% of cases. Other gut abnormalities and cardiovascular abnormalities are also commonly present.

Duodenal atresia is rapidly fatal unless diagnosed promptly and treated surgically without delay; otherwise the electrolyte and fluid balance deteriorates rapidly. There are two major factors associated with survival, a high birthweight and lack of associated anomalies.

CASE REPORTS

Case 1

A 15-year-old was referred for ultrasound late in pregnancy because the LMP was not known. On clinical examination, the fundus corresponded to 36 weeks, although the fetus felt smaller and freely mobile. Ultrasound examination showed a single live fetus with a BPD corresponding to 31 weeks' gestation. Gross hydramnios was noted. The fetal cerebral ventricles and spine appeared normal. Within the upper fetal abdomen, double cystic structures were clearly visualized (Fig. 1). Two normal kidneys were demonstrated in the fetus, and the fetal bladder was full at the time of examination. Oblique scans through the upper abdomen of the fetus clearly showed that the double cystic structures were connected (Fig. 2). A firm diagnosis of duodenal atresia was made at this time.

The patient went into premature labour two weeks later. A naso-gastric tube was passed immediately following birth and the stomach contents aspirated. Supine X-rays of the abdomen six hours after birth showed the stomach and the duodenum to be distended with gas, with no gas present in the distal bowel (Fig. 3). This radiographic appearance is typical of duodenal atresia. The child was taken to theatre and the atresia was relieved.

Case 2

A 26-year-old Indian patient attended for an ultrasound scan at 18 weeks gestational age. The scan demonstrated a single fetus with a biparietal diameter measurement consistent with dates, the fetal anatomy appeared normal, as did the quantity of liquor present.

The patient was rescanned at 29 weeks as part of a project on fetal growth patterns in Indian patients. Gross hydramnios was present, and two large fluid-filled structures were seen in the fetal abdomen. The fetal kidneys and bladder were seen as separate, normal structures and the BPD measurement was within normal limits. Because of the two fluid-filled structures in the fetal abdomen, "the double bubble sign", together with the presence of hydramnios, the diagnosis of duodenal atresia was considered, and the patient re-booked for a scan three weeks later.

On this occasion, the two fluid-filled structures were still present (Fig. 4) and, on performing oblique scans, it was possible to demonstrate the connection between the two "bubbles" (Fig. 5). The fetal kidneys and bladder were

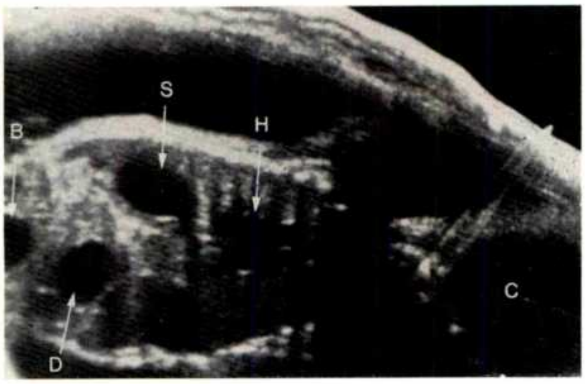


FIG. 1.

Longitudinal scan through the fetal trunk showing the heart (H) within the thorax. Double cystic structures (S and D) are seen in the upper abdomen and the top of the bladder (B) can be seen just on the picture. (C) fetal head.

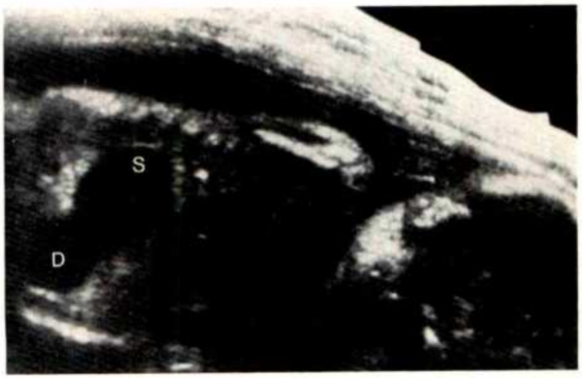


FIG. 2.

A longitudinal oblique scan through the fetal trunk showing that the double cystic structures connect and have the typical appearance of stomach (S) and duodenum (D).

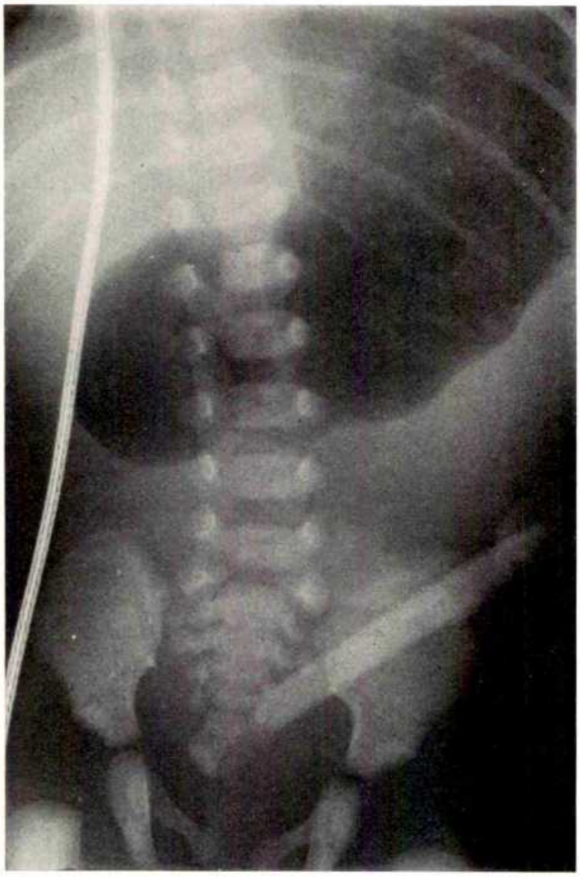


FIG. 3.
A supine radiograph of the baby's abdomen taken after intubation of the stomach. This shows the stomach to be full of air with no evidence of air in the distal bowel.

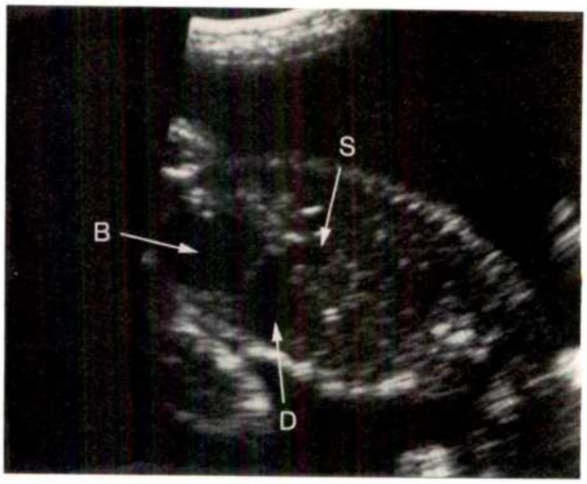


FIG. 5.
Oblique scan through the same fetus showing the duodenum (D) and stomach (S) connecting. The fetal bladder (B) is also demonstrated.

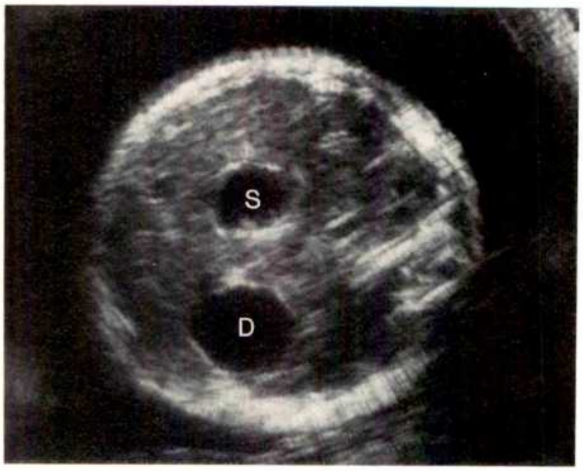


FIG. 4.
Transverse scan through the upper fetal abdomen showing double cystic structures (S and D).

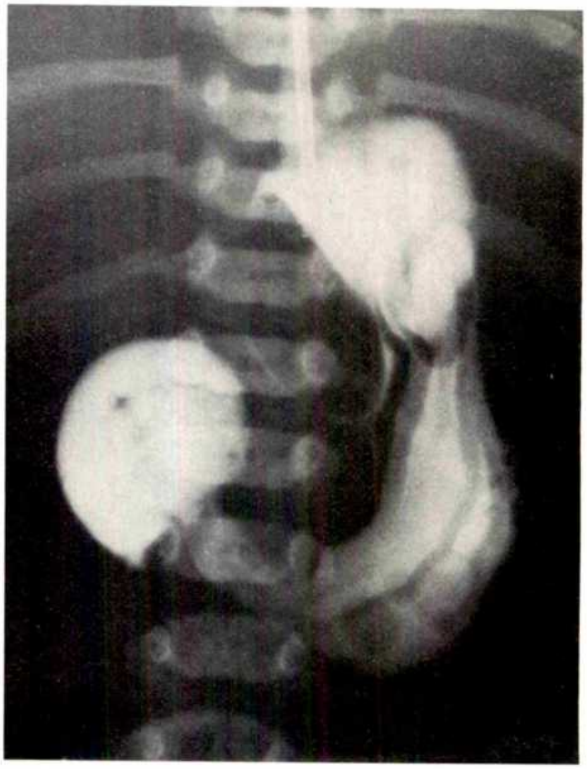


FIG. 6.
A supine radiograph of the baby's abdomen after injection of constrast medium.

again visualized and appeared normal. Gross hydramnios was still present and causing the patient some discomfort.

Four weeks later the patient attended the antenatal clinic for her 36-week check-up and informed the doctor that she had lost some liquor vaginally several days previously. Clinically, the obstetrician did not think that this was so and apart from the hydramnios, he found nothing to worry about and the patient was sent home. Two weeks later the patient was admitted in labour, and a still-born infected infant was delivered. The infant was radiographed after injection of contrast medium and the classical appearance of duodenal atresia was demonstrated (Fig. 6). This finding was confirmed at post-mortem.

Discussion

Antenatal recognition of fetal abnormality such as this allows prompt treatment following birth.

Since 1975, there have been at least ten ultrasound case reports describing the appearance of duodenal atresia, the first being that of Loveday *et al.* (1975), where bistable images were obtained, showing no detail of the soft tissue structures. The finding of double cystic structures in the fetal abdomen is associated with several possible fetal abnormalities. The first is duodenal atresia, as described here and elsewhere (Gee and Abdullah, 1978). A similar appearance is produced by bilateral hydronephrosis. A case with ultrasonic findings like this has recently been reported (Hately and Nicholls, 1979). One of us has recently reported a case of a choledochal cyst (Dewbury *et al.*, 1980), in which the initial ultrasound appearance at 32 weeks of gestation also showed double cystic structures in the abdomen. One of these represented the choledochal cyst itself, and the other the fluid-filled stomach. On the follow-up scans two weeks later, the choledochal cyst remained unchanged in appearance but the stomach was then almost empty, and only a single cystic structure remained in the abdomen.

If the double cystic structures can be seen to connect by oblique scans, as is shown in both these cases (this is particularly easily done with real time), a firm diagnosis of duodenal atresia can be made, as this distinguishes this condition from the other possibilities that have been mentioned.

It is interesting to note that the second case was scanned at 18 weeks, when the stomach appeared normal in size and there was a normal quantity of liquor present. It is therefore probably not possible to diagnose or exclude the presence of duodenal atresia early in pregnancy.

It should also be remembered that even if this condition is diagnosed antenatally, there is a 50% chance of another significant abnormality being present and a 33% chance of Down's syndrome.

REFERENCES

Dewbury, K. C., Aluwihare, A. P. R., Birch, S. J. and Freeman, N. V., 1980. Antenatal ultrasound demonstration of a choledochal cyst. *British Journal of Radiology*, *53*, 906–907.

Fonkalsrud, E. W., De Lorimier, A. A. and Hays, D. M., 1969. Congenital atresia and stenosis of the duodenum—a review. *Pediatrics*, *43*, 79–83.

Gee, H. and Abdullah, U., 1978. Antenatal diagnosis of fetal duodenal atresia by ultrasonic scan. *British Medical Journal*, *ii*, 1265.

Hately, W. and Nicholls, B., 1979. The ultrasonic diagnosis of bilateral hydronephrosis in twins during pregnancy. *British Journal of Radiology*, *52*, 989–990.

Irving, I. M. and Rickham, P. P., 1978. Duodenal atresia and stenosis: annular pancreas. In *Neonatal Surgery*. Ed. Rickham *et al.* (Butterworths, London), pp. 335–370.

Loveday, B. J., Barr, J. A. and Aitken, J., 1975. The intrauterine demonstration of duodenal atresia by ultrasound. *British Journal of Radiology*, *48*, 1031–1032.

1981, *British Journal of Radiology*, *54*, 636–637

Short communication

Simplified cell labelling with indium-111 acetylacetonate and indium-111 oxinate

By W. Th. Goedemans, Ph.D.

Byk-Mallinckrodt CIL B.V., P.O. Box 3, 1755 ZG Petten, The Netherlands

(*Received August 1980 and in revised form December 1980*)

Cell labelling by means of chelated ^{111}In has been reported to be a useful clinical tool in the diagnosis of abscesses (Thakur *et al.*, 1977). ^{111}In oxinate (oxine) can label the cellular blood components granulocytes (Segal *et al.*, 1976; Goedemans *et al.*, 1980), lymphocytes (Lavender *et al.*, 1977), platelets (Thakur *et al.*, 1976; McIlmoyle *et al.*, 1977; Wistow *et al.*, 1978; Scheffel *et al.*, 1979) and erythrocytes (Thakur, 1977). These cells have been used to locate abscesses and inflammatory reactions, myocardial infarctions, thrombus formation, rejection of transplanted organs etc. For some time, labelled erythrocytes have been extensively used for blood volume measurement. ^{111}In-labelled erythrocytes show cardiac, liver and spleen blood pool activity 24 hours after intravenous administration. ^{111}In oxinate red cells provide a potential method for detection of intermittent gastrointestinal bleeding (Winzelberg *et al.*, 1980).

It has been suggested (Sinn and Silvester, 1979) that acetylacetone has an advantage over oxine with regard to cell toxicity due to the presence of ethanol in the oxine preparation and also that oxine itself could be toxic at high concentrations.

This publication draws attention to the fact that recently aqueous ^{111}In oxinate preparations without ethanol have been developed with an oxine concentration as low as 25 μg per mCi ^{111}In. The effect of different oxine and ethanol concentrations on the viability of polymorphonuclear leukocytes has been described in the literature and it is shown that 25 μg oxine does not decrease cell viability (Zakhireh *et al.*, 1979). Furthermore, based on experimental evidence, oxine has an advantage over acetylacetone with regard to cell labelling yield especially if the aspect of concentration of both chelating agents is included in the comparison.

MATERIALS AND METHODS

The following materials were used. $^{111}InCl_3$ solution. This consisted of "carrier free" $^{111}InCl_3$ in 0.09–0.11 *N* hydrochloric acid, heat sterilized (Byk-Mallinckrodt).

TRIS-acetate buffered ^{111}In acetylacetone: seven different ^{111}In acetylacetonate preparations were made containing acetylacetone in the following concentrations: 3 mg/ml (original concentration used by Sinn and Silvester, 1979), 1.5 mg/ml, 0.3 mg/ml, 0.15 mg/ml, 75 μg/ml, 30 μg/ml and 15 μg/ml. All preparations contained 0.024 *N* hydrochloric acid, 5.6 mg sodium chloride, 4.1 mg sodium acetate and 37 MBq (1 mCi) ^{111}In per millilitre 3.025 mg TRIS (Baker). The preparations had a pH of 6.5 and a tonus of 305–280 mOsmol/kg.

TABLE I

Total amount of chelating compound (μg)	Labelling efficiency (%)
3000 acetylacetone	88.0
1500 acetylacetone	55.0
300 acetylacetone	15.0
150 acetylacetone	17.0
75 acetylacetone	12.7
30 acetylacetone	11.4
15 acetylacetone	12.8
25 oxine	92.0

TRIS-acetate-buffered ^{111}In oxinate: This consisted of a heat-sterilized, ready for use preparation (Byk-Mallinckrodt) containing 3.025 mg TRIS, 0.024 *N* hydrochloric acid, 5.6 mg sodium chloride, 4.1 mg sodium acetate, 25 μg oxine (Baker) and 37 MBq (1 mCi) ^{111}In per millilitre. The pH was 6.5 and the tonus 280 mOsmol/kg (isotonic solution).

The cell suspension was prepared by suspending washed bovine erythrocytes in saline at a concentration of 6×10^{11} cells per litre (Coulter Counter). Cell labelling was carried out simply by adding and mixing 4 ml of cell suspensoin to 1 ml ^{111}In acetylacetonate or ^{111}In oxinate. Incubation was carried out at room temperature for 15 minutes. The labelling efficiencies were determined by measuring the radioactivity of the cell fraction after centrifuging the suspension.

RESULTS

Table I shows the effect of different concentrations of chelating compound on the cell labelling efficiency. The amounts shown represent the amounts of chelating compound in the initial oxine or acetylacetone preparations. The concentrations in the final cell suspensions expressed as μg/ml were a factor of five lower. The concentration of acetylacetone has to be 120 times higher than that of oxine to obtain a labelling yield which comes close to that of oxine. If one should make the comparison between the two chelating compounds on a molecular weight basis instead of the weight basis, the differences in concentration at which comparable labelling efficiencies would be obtained are even bigger; the factor 120 would become 174.

DISCUSSION

The LC_{50} of acetylacetone in rats is 1000 mg/kg (Spector, 1956). Relating this LC_{50} to the LD_{50} of oxine in mice, 48 mg/kg (Bernstein *et al.*, 1963), there is an advantage of a factor of 21 with acetylacetone in terms of toxicity. However, the labelling potential differs by a factor of 120 in advantage of oxine. So the toxicity of ^{111}In acetylacetonate is not less than ^{111}In oxinate in concentrations resulting in comparable labelling yields. As aqueous ^{111}In oxinate is available without ethanol or any other additive except buffer, the labelling of cells is also reduced to a one-step operation.

REFERENCES

BERNSTEIN, E. H., PIENTA, P. W. and GERSHON, H., 1963. Acute toxicity studies on 8-quinolinol and some derivatives. *Toxicology and Applied Pharmacology*, *5*, 599–604.

GOEDEMANS, W. Th., HARDEMAN, M. R. and BELFER, A. J., 1980. Comparison of Indium-111 oxinate labelled autologous granulocytes with Indium-111 oxinate and Indium-111 chloride as abscess scanning agents. An experimental study in an animal model. *European Journal of Nuclear Medicine*, *5*, 63–68.

Lavender, J. P., Goldman, J. M., Arnot, R. N. and Thakur, M. L., 1977. Kinetics of indium-111 labelled lymphocytes in normal subjects and patients with Hodgkins disease. *British Medical Journal*, *ii*, 797–799.

McIlmoyle, G., Davis, H. H., Welch, M. J., Primeau, J. L., Sherman, L. A. and Siegel, B. A., 1977. Scintigraphic diagnosis of experimental pulmonary embolism with In-111-labelled platelets. *Journal of Nuclear Medicine*, *18*, 910–914.

Scheffel, U., Tsan, M. and McIntyre, P. A., 1979. Labeling of human platelets with (^{111}In)8-hydroxyquinoline. *Journal of Nuclear Medicine*, *20*, 524–531.

Segal, A. W., Arnot, R. N., Thakur, M. L. and Lavender, J. P., 1976. Indium-111 labelled leukocytes for localisation of abscesses. *Lancet*, *ii*, 1056–1058.

Sinn, H. and Silvester, D. J., 1979. Simplified cell labelling with indium-111 acetylacetone. *British Journal of Radiology*, *52*, 758–759.

Spector, W. S. (Ed.), 1956. *Handbook of Toxicology*. Vol. I. (Saunders, Philadelphia), pp. 346–347.

Thakur, M. L., Welch, M. J., Joist, J. H. and Coleman, R. E., 1976. Indium-111 labeled platelets: Studies on preparation and evaluation of in vitro and in vivo functions. *Thromb. Research*, *9*, 345–357.

Thakur, M. L., 1977. Gallium-67 and indium-111 radiopharmaceuticals. *International Journal of Applied Radiation*, *28*, 183–201.

Thakur, M. L., Lavender, J. P., Arnot, R. N., Silvester, D. J. and Segal, A. W., 1977. Indium-111 labeled autologous leukocytes in man. *Journal of Nuclear Medicine*, *18*, 1012–1019.

Winzelberg, G. G., Castronovo, F. P., Callahan, R. J., McKusick, K. A. and Strauss, H. W., 1980. ^{111}In oxine labeled red cells for detection of simulated lower gastrointestinal bleeding in an animal model. *Radiology*, *135*, 455–461.

Wistow, B. W., Grossman, Z. D., McAffee, J. G., Subramanian, G., Henderson, R. W. and Roskopf, M. L., 1978. Labeling of platelets with oxine complexes of Tc-99m and In-111. Part 1. In vitro studies and survival in the rabbit. *Journal of Nuclear Medicine*, *19*, 483.

Zakhireh, B., Thakur, M. L., Malech, H. L., Cohen, M. S., Gottschalk, A. and Root, R. K., 1979. Indium-111-labeled human polymorphonuclear leukocytes: viability, random migration, chemotaxis, bactericidal capacity and ultrastructure. *Journal of Nuclear Medicine*, *20*, 741–747.

Book review

Optimization of Radiotherapy. Pp. 89, 1980 (World Health Organization Technical Report Series 644). (WHO, Geneva), Sw. fr. 6.
ISBN 92-4-120644-6

This modest-seeming little book contains much sound sense and repays careful reading. This is perhaps surprising, since it comes from a committee, and much praise is therefore due to the chairman Professor J. S. Mitchell and the rapporteur Professor Walstam from Stockholm, aided no doubt by the international group of investigators with a strong core from Cambridge and London. The report consists of six chapters outlining the organization of radiotherapy centres and gives much detail of equipment and dosimetry. There is a very fine summary of practical radiobiology, discussing dose–time factors and fractionation. There is a very interesting annexe of forms and codes for radiotherapy data reporting. These are only two particularly good parts of this interesting report—it is well worthwhile obtaining the booklet itself (subscription for 15 to 20 such reports is only 80 Swiss francs) and finding out more for oneself. Our taxpayers' money has been well spent.

K. E. Halnan.

Draft British Standard

Methods of Leak Testing for Sealed Radioactive Sources. Draft for Development, British Standards Institution DD66: 1980, pp.i+3, £5·00.

The draft has been prepared under the direction of the Nuclear Engineering Standards Committee and is based on Technical Report 4826-1979 by Technical Committee 85 of the International Organization for Standardization.

It is emphasized in the preamble that this publication is of a provisional nature because of the lack of practical experience in the use of the leak-test methods described. It is not to be regarded as a British Standard but the BSI recommended that it should be applied on a provisional basis so that information and experience of its practical application may be obtained. A review of the draft should be made not later than two years after its publication and comments are invited by the BSI from persons interested in this subject.

The draft covers leak tests using both radioactive and non-radioactive methods. The radioactive tests covered are the wipe test (smear), dry wipe, immersion, boiling immersion gaseous emanation (for ^{226}Ra sources) and liquid scintillant emanation. The non-radioactive methods are the vacuum bubble test, hot liquid bubble test, gas pressurization test, helium test, helium pressurization test and the water pressurization test. A table is given comparing the various leak test methods and the acceptance thresholds.

T. J. Davey.

1981, *British Journal of Radiology*, 54, 638–639

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

The oncogenic potential of X rays and/or hyperthermia in C3H-10T½ cells

THE EDITOR—SIR,

Since hyperthermia is being used extensively in cell biology studies and as a tool for cancer therapy with or without irradiation (Proc. Int. Cancer Symposium on Cancer Therapy by Hyperthermia and Radiation, 1975; Streffer *et al.*, 1978; Dewey *et al.*, 1979), it is important to determine whether heat treatment can cause oncogenic transformation.

In a recent article by Harisiades *et al.* (1980), it was shown that heat treatment alone in the temperature range 40.0–45.0°C did not cause oncogenic transformation in cultured C3H-10T½ cells, while heat treatments in the temperature range 40.0–42.2°C reduced the incogenic transformation frequency resulting from X rays when heating was performed immediately after X irradiation. We have also investigated the effect of heat alone or combined with X rays on induction of oncogenic transformation in the C3H-10T½ cell system developed by Reznikoff *et al.* (1973a; b). These data were first presented at the 28th Annual Meeting of the Radiation Research Society (Raaphorst *et al.*, 1980). We have used experimental protocols which include heating either before or after X irradiation such that the two treatments were done one immediately after the other or separated by an incubation interval at 37°C.

The C3H-10T½ cells were cultured in Basal Medium Eagles supplemented with 10% fetal calf serum containing no antibiotics. The transformation assay was carried out using exponentially growing C3H-10T½ cells with passage numbers below 15. The standard techniques and scoring criteria set forth by Reznikoff *et al.* (1973a; b) were used. The cells were exposed in suspension and then plated into Falcon T75 flasks. Heating was performed using a thermally regulated waterbath and irradiation was carried out on a Siemens Stabilipan 2 X-ray machine operating at a dose rate of 300 cGy (rad)/min.

The results are presented in Table I. The data show that heating at 42°C for 60 min did not induce cell transformation. Also, heating for 5 min at 45°C or 180 min at 41.5°C (data not shown) did not significantly increase the transformation frequency per viable cell (TF/VC) with respect to the control which is in agreement with the data of Harisiadis *et al.* (1980). For irradiation alone (4.0 Gy) the (TF/VC) was about 9×10^{-3} and this was confirmed in five separate experiments. When the heat and radiation treatments were combined, the TF/VC was not significantly increased when irradiation was done during or immediately before or after a 1 h heating interval at 42°C. The data of Harisiadis *et al.* (1980) and Miller *et al.* (1979) show a decrease in transformation frequency when a heat exposure at 40.0–42.2°C followed immediately after irradiation. However, in our experiments, when an incubation interval was introduced between the two treatments (Table I) there was a significant increase in the TF/VC for the 60 min incubation intervals. For the combination treatment of X irradiation and heating for 1 h at 42°C, this increase was observed in three separate experiments for a 10 min or a 60 min incubation interval between treatments. In addition, for heating at 45°C for 5 min or 41.5°C for 180 min (data not shown) increases in the TF/VC were also observed when a 4.50 Gy dose preceded or followed heating by a 10 min incubation interval at 37°C. The number of transformants counted, the survival after each treatment, the number of viable cells per Falcon T75 flask, the total number of cells at risk and the transformation frequency per cell at risk are also given.

TABLE I

SURVIVAL AND TRANSFORMATION OF C3H-10½ CELLS BY HYPERTHERMIA AND X RAYS

Treatment[3]	Average viable cells per T75	Survival percent[1,4]	Total No. of cells at risk[6]	No. of transformed foci[2]	Transformation frequency	
					Per viable cell[5]	Per cell at risk
No treatment	248	100 (1.4)	3226	0	$< 3.1 \times 10^{-4}$	$< 3.1 \times 10^{-4}$
△	257	69.0 (0)	4466	0	$< 3.2 \times 10^{-4}$	$< 2.24 \times 10^{-4}$
○	69	27.3 (1.1)	3226	8	8.89×10^{-3} (2.0)	2.48×10-3
□	136	2.10 (0.48)	74449	26	1.36×10^{-2} (0.29) NS	3.49×10^{-4}
△ 30 sec ○	172	2.77 (0.12)	68245	17	8.99×10^{-3} (2.6) NS	2.49×-10^{-4}
○ 30 sec △	160	2.60 (0.056)	68245	18	1.02×10^{-2} (0.21 NS)	2.63×10^{-4}
△ 60 min ○	158	5.09 (0.016)	34122	25	1.59×10^{-2} (0.23) $p < 0.025$	7.62×10^{-4}
○ 60 min △	148	4.70 (0.90)	40327	38	2.00×10^{-2} (0.23) $p < 0.005$	9.35×10^{-4}

[1] All survival was normalized to the plating efficiency of 12.3%.

[2] Both type II and III foci were scored.

[3] △ = 42°C for 1 hr; ○ = 4.00 Gy; □ = X irradiation during heating.

[4] The standard error of the mean is shown in parentheses, based on the mean per flask.

[5] Level of significance of the difference with respect to X ray alone is given in column 6 (NS = not significant).

[6] Total number of cells plated multiplied by the plating efficiency.

These data may have important clinical implications in that hyperthermia by itself induces no increase in transformation frequency, and may thus be a non-carcinogenic mode of cancer treatment unlike other forms of therapy such as radiation or many of the chemicals used in chemotherapy. When heat at 42°C and radiation were administered simultaneously or immediately following one another, no significant increase in transformation was observed and therefore this may be a preferred therapy protocol for the combined treatments. In addition, the survival was the lowest for these treatment protocols. Even though the combination of hyperthermia and radiation did enhance the TF/VC when incubation at 37°C occurred between treatments, if one looks at the data in terms of transformation frequency per cell at risk, the frequency was lower for all the combined treatments compared with X rays alone. This was so because more cell killing resulted from the combined treatments compared with X rays alone and with application to therapy this may be the more appropriate way to view the data.

Yours etc.,

G. P. RAAPHORST,
E. I. AZZAM,
M. D. SARGENT,
M. EINSPENNER,
J. BORSA.

Medical Biophysics Branch,
Atomic Energy of Canada Research Company,
Whiteshell Nuclear Research Establishment,
Pinawa, Manitoba, Canada ROE 1LO.

(*Received August 1980 and in revised form January 1981*)

REFERENCES

DEWEY, W. C., FREEMAN, M. L., RAAPHORST, G. P., CLARK, E. P., WONG, R. S. L., HIGHFIELD, D. P., SPIRO, I. J., TOMASOVIC, S. P., DENMAN, D. L. and COSS, R. A., 1979. Cell biology of hyperthermia and radiation. In *Radiation Biology and Cancer Research*, Ed. by R. E. Meyn and H. R. Withers (Raven Press, New York), pp. 589–621

HARISIADIS, L., MILLER, R. C., HARISIADIS, S. and HALL, E. J., 1980. Oncogenic transformation and hyperthermia. *British Journal of Radiology*, *53*, 479–482.

MILLER, R. C., HARISIADIS, L., HARISIADIS, S. and HALL, E. J., 1979. Hyperthermia and X-irradiation; their effect on the induction of oncogenic transformation. *6th International Congress of Radiation Research, Tokyo* (abstract), p. 232.

Proceedings of the International Symposium Therapy by Hyperthermia and Radiation, 1975. (National Cancer Institute–College of Radiology, Washington, DC.)

REZNIKOFF, C. A., BRANKOW, D. W. and HEIDELBERGER, C., 1973a. Establishment and characterization of a cloned line of C3H mouse embryo cells sensitive to postconfluence inhibition of division. *Cancer Research*, *33*, 3231–3238.

REZNIKOFF, C. A., BERTRAN, J. S., BRANKOW, D. W. and HEIDELBERGER, C., 1973b. Quantitative and qualitative studies of chemical transformation of cloned C3H mouse embryo cells sensitive to postconfluence inhibition of cell division. *Cancer Research*, *33*, 3239–3249.

STREFFER, C., VAN BEUNINGEN, D., DIETZEL, F., ROTTINGER, E., ROBINSON, J. E., SCHERER, E., SEEBER, S. and TROTT, K. R. (Eds.), 1978. *Cancer Therapy by Hyperthermia and Radiation* (Urban & Schwarzenberg, Baltimore/Munich).

Whither the röntgen?

THE EDITOR—SIR,

We are watching the fall of the röntgen with much concern. Will it be replaced by $\mathrm{C\,kg^{-1}}$, air kerma, $\mathrm{J\,kg^{-1}}$ or grays in air? We strongly support the first which has also recently been advocated by the DHSS following an EEC directive (80/181/EEC). The DHSS document (RScO 29/6) says "the SI unit of exposure is the $\mathrm{Ckg^{-1}}$ which will replace the röntgen. No special name has been assigned to this unit and its use is expected to decrease".

We consider that the use of both grays in air and grays in tissue or water would be a retrograde step and would be no advance on the present clinical situation where there has been much confusion between the röntgen and the rad. The obvious abbreviation will be just grays with no specification of absorber, leaving the reader or listener to interpret as grays in tissue. The area of concern is that of dose specification in radiotherapy where the intercomparison of dose regimes between different departments and different countries needs to be unequivocal and not open to incorrect interpretation. A difference of 10% is irrelevant in radiological protection, but critical in radiotherapy.

There seems to be a strong lobby from the "purists" for the use of air kerma with the units of grays in air. We think there are a lot of ordinary folk (like us) who don't know quite what kerma is anyway and will just get confused. We think that there is a good case for having coulombs per kilogram as an "absolute" exposure standard and to transfer straight to grays in tissue for absorbed dose.

These considerations are particularly important in the specification of teletherapy and interstitial sources, where the problem is what to specify at a distance. We join those who suggest the concept of absorbed dose in a small element of tissue "free in air" or *vacuo*. This is an artificial, but necessary concept, since for teletherapy sources one normally allows for absorption and backscatter to get to a "useful" absorbed dose, whereas for interstitial sources there is in addition a large inverse-square law factor and possibly a small air-attenuation correction. We know the idea of absorbed dose in an element of tissue in air is a strange one, but we think the use of air kerma is even less related to a practical situation.

We should also like to comment on the recent BCRU memorandum (1980) with regard to the proposed calibration depths for various X-ray beam energies (Table I, *loc. cit.*). The inclusion of another calibration depth at 20 mm for 150 kV–400 kV beams we feel is not needed, and it is probably best left at 50 mm for 150 kV–10 MV. We do not use it at present and feel it confuses rather than clarifies the situation. The other suggested depths of 0.07 mm for 10–100 kV and 10 mm for 50–150 kV X-ray beam calibrations may be an improvement on an in-air calibration, but might present difficulties in practice for the following reason. The percentage depth-dose change in tissue across the size of a thimble chamber at orthovoltage energies will be large, of the order of 20% at 10 mm depth for an 80 kV beam. Therefore the positioning reproducibility of the chamber will be difficult in such a fast changing gradient. The fact that the new NPL secondary standard chamber is of different physical dimensions from the Farmer chamber normally used for clinical calibrations makes this situation worse.

What do other readers feel about the problems raised here? Would they support the use of the $\mathrm{C\,kg^{-1}}$, or the air kerma, to replace the röntgen? The previous generation has been bedevilled by the röntgen and the rad. Do we have to bedevil the next one by the gray in air and the gray in tissue?

Yours, etc.,

B. STEDEFORD,
A. DIXON-BROWN.

Department of Radiation Physics,
Churchill Hospital,
Headington, Oxford OX3 7LJ.

(*Received April 1981*)

REFERENCE

BRITISH COMMITTEE ON RADIATION UNITS AND MEASUREMENTS, 1980. Quantities for reporting the calibration of therapy-level dosemeters in photon beams. *British Journal of Radiology*, *53*, 917–918.

1981, *British Journal of Radiology*, *54*, 640

Analysis of publications, 1978, 1979 and 1980

The tables below give analyses of papers which appeared in volumes 51 to 53 of THE BRITISH JOURNAL OF RADIOLOGY (1978, 1979, 1980). They are in the same form as the tables for volumes 49 and 50, which appeared on page 609 of Volume 50 and page 601 of Volume 51. Short communications are now included. There have been no papers on thermography but two new categories have been introduced: nuclear magnetic resonance and hyperthermia. Over the period of five years the main change has been a slight diminution in the number of contributions relating only to diagnosis by X rays, with a compensating increase in ultrasonics and hyperthermia.

Category	Number of contributions	Number of pages	Pages per contribution	Per cent of total	
				Contributions	Pages
Volume 51, 1978					
Diagnosis by X rays excluding case reports	59	329	5.6	32	39
Case reports (X-ray diagnosis)	24	51	2.1	13	6
Diagnosis by ultrasonics	11	29	2.6	6	3
Diagnosis by nuclear medicine	14	65	4.6	8	8
Nuclear magnetic resonance	2	10	5.0	1	1
Radiotherapy	14	95	6.8	8	11
Physics	18	94	5.2	10	11
Radiobiology	20	99	5.0	11	12
Hyperthermia	6	31	5.2	3	4
Radiation hazards	5	17	3.4	3	2
Nuclear medicine with physics	2	12	6.0	1	2
X-ray diagnosis with physics	3	7	2.3	2	1
Radiotherapy with physics	0	0	—	0	0
Ultrasonics with others	1	4	4.0	1	0
Other combinations	2	4	2.0	1	0
Total	181	847	4.7	100	100
Volume 52, 1979					
Diagnosis by X rays excluding case reports	42	222	5.3	23	26
Case reports (X-ray diagnosis)	32	76	2.4	18	9
Diagnosis by ultrasonics	16	74	4.6	9	9
Diagnosis by nuclear medicine	12	47	3.9	7	6
Nuclear magnetic resonance	2	10	5.0	1	1
Radiotherapy	11	56	5.1	6	7
Physics	12	67	5.6	7	8
Radiobiology	16	83	5.2	9	10
Hyperthermia	8	41	5.1	4	5
Radiation hazards	7	52	7.4	4	6
Nuclear medicine with physics	5	25	5.0	3	3
X-ray diagnosis with physics	2	14	7.0	1	2
Radiotherapy with physics	4	14	3.5	2	2
Ultrasonics with others	4	21	5.3	2	2
Other combinations	8	33	4.1	4	4
Total	181	835	4.6	100	100
Volume 53, 1980					
Diagnosis by X rays excluding case reports	49	129	2.6	21	15
Case reports (X-ray diagnosis)	39	89	2.3	17	10
Diagnosis by ultrasonics	25	72	2.9	11	8
Diagnosis by nuclear medicine	21	97	4.6	9	11
Nuclear magnetic resonance	1	2	2.0	–	–
Radiotherapy	10	47	4.7	4	5
Physics	18	74	4.1	8	9
Radiobiology	21	124	5.9	9	14
Hyperthermia	6	27	4.5	2	3
Radiation hazards	6	39	6.5	3	5
Nuclear medicine with physics	7	34	4.9	3	4
X-ray diagnosis with physics	11	48	4.4	5	6
Radiotherapy with physics	7	19	2.7	3	2
Ultrasonics with others	8	33	4.1	3	4
Other combinations	5	36	7.2	2	4
Total	234	870	3.7	100	100

Forthcoming events

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

First International Symposium on Minimal Invasive Cancer

Organized by the University Clinic of Obstetrics and Gynaecology, Graz, Austria, to be held at the Kongresshaus, Graz, July 1–4, 1981. Language: English. Main topics: cervix, vulva, endometrium, breast, oesophagus, stomach, large intestine, lung, thyroid, urinary bladder, prostate, larynx, oral cavity, skin, other organs. Enquiries: Interconvention, PO Box 105, A-1014, Vienna, Austria (phone (0222) 57 62 88). President: Prof. E. Burghardt; Secretary General, Dr. E. Holzer.

Tenth L. H. Gray Conference

Will be held in Oxford on July 13–16, 1981 on "biological actions of radiofrequency, microwave and ultrasonic radiations".

A conference to review and discuss past and current research on the radiobiology and biophysics of the radiations, particularly in relation to their potential therapeutic value.

Information/Chairman of Organizing Committee: Dr. C. R. Hill, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey.

Radionuclides in Nephrology
Fifth Internatioval Symposium

September 2–4, 1981 at the Royal Society, London. Further details from A. R. Constable, Institute of Urology, 172 Shaftesbury Avenue, London WC2 8JE.

International Symposium and Course on Abdominal Ultrasound

Turku, Finland, August 10–12, 1981, organized by the Radiological Society of Finland and the European Association of Radiology. Language: English. Guest speakers: C. R. Hill, H. H. Holm, M. Johnson, A. Kratochwil, C. Metreweli, E. H. Smith and F. Weill. Two "free communications" sessions, for which 10 minute papers are invited: abstracts to be submitted with registration. Technical exhibition and social programme. Information and registration: Oy Konfer Ab, Yliopistonkatu 29 c B, SF-20100 Turku 10, Finland.

Society of Nuclear Medicine Europe
19th Annual Congress

September 8–11, 1981. Information: President Dr. H. Rösler, Department of Nuclear Medicine, Inselspital, 3010 Bern, Switzerland.

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275–2617.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D., Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

The Faculty of Radiologists of The Royal College of Surgeons in Ireland

21st Anniversary Meeting, Dublin, October 2–3, 1981: jointly with The British Institute of Radiologists, The Royal College of Radiologists, and The Royal Society of Medicine. Diagnostic and therapy sessions; topics to include radiology in renal failure and radiology of trauma. The BIR Presidential Address for 1981, "Chest radiology—guesswork or science?" will be given by Dr. D. H. Trapnell. Technical exhibition. Details: Miss A. Daly, Faculty of Radiologists, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

The Mayneord Symposium

Friday, February 19, 1982. This meeting is being organized by, the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. It will be an all-day meeting to be held at the Royal Society, in Carlton House Terrace, London. The theme for the meeting will be "The future in radiology" as seen by distinguished workers in a number of branches of radiological science.

Forthcoming events

SYMPOSIUM ON EDUCATION AND TRAINING IN RADIOBIOLOGY

Dresden, May 12–15, 1982. Organized by the Gesellschaft für medizinische Radiologie der DDR, under the auspices of the European Society of Radiology. Languages: English, French and German. Registration by December 1, 1981; papers by August 15, 1981. Information: Professor R. Barke, Radiologische Klinik, DDR – 8019, Dresden, Fetscherstrasse 74.

THE RADIOLOGICAL DIAGNOSIS AND TREATMENT OF THYROID DISEASE

WEDNESDAY, NOVEMBER 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held in London (venue to be announced). The meeting will cover all aspects of thyroid disease, including the use of isotopes. There will be some invited speakers but proffered papers are invited and should be sent to: Dr. John Frank, The Wessex Regional Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY before August 31, 1981.

BRITISH MEDICAL ULTRASOUND SOCIETY

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1. Proffered papers are invited; abstracts should be sent to Dr. W. Hately, X-ray Department, London Hospital, Whitechapel, London E1 1BB to arrive not later than August 31, 1981.

PAEDIATRIC RADIOLOGY 1981

GREAT ORMOND STREET, LONDON, NOVEMBER 26–27

This annual two-day course is designed for consultants and senior registrars. The theme will be the gut; other topics covered will include jaundice, hypertension and the neonatal big head. Speakers will include paediatricians, paediatric surgeons and endoscopists; there will be opportunity for open discussion.

There are a limited number of places. Cost £40. Full details: Dr. I. Gordon, Department of Paediatric Radiology, Hospital for Sick Children, Great Ormond Street, London WC1 (telephone 01-405 9200).

COMPUTERS IN RADIATION ONCOLOGY IN EUROPE—III

USE OF COMPUTERS IN CLINICAL CANCER RECORDS

A workshop will be held at the headquarters of the World Health Organization, Geneva, April 26–28, 1982, organized by the Commission Informatique of the European Association of Radiology in co-operation with the World Health Organization (WHO), the International Union Against Cancer (UICC) and the European Society for Therapeutic Radiology and Oncology (ESTRO), limited to 120 members.

The three official languages of EAR may be used, but the preferred language of the workshop will be English. No simultaneous translation will be available. Proferred papers of *circa* 15 minutes' duration are invited on the following topics:

1. Population based cancer registries; (a) aims; (b) experience, present systems; (c) quality control; (d) new systems, possibilities and limitations.
2. Hospital based cancer registries: (a) aims; (b) minimal variates for cancer registry—disease and treatment; (c) experience in the five years since the Vienna workshop; (d) feedback—what information does the clinician want? What can he get? (e) impact of technological change in past five years.
3. Tumour based cancer registries and data centres for clinical trials.
4. Administrative/occupation based registries.
5. Co-ordination of registry data: (a) confidentiality and ethical aspects; (b) managerial aspects, administrative, legal and financial; (c) technological aspects.

This meeting is designed to facilitate communication between European clinical oncologists and cancer statisticians and to probe the "state of the art" in interaction between doctor and data. In particular, reports are sought of hospital-based cancer record systems which have been in use since the past workshop held in Vienna five years ago and on new developments in computer hardware and software that make modern improved hospital cancer records possible.

Brief (50 words) abstracts of proferred papers are to be submitted by October 1, 1981 to a member of the Organizing Committee: Professor R. J. Berry, Department of Oncology, The Middlesex Hospital Medical School, London W1P 7PN, England; Dr. J. Gary-Bobo, Centre Paul Lamarque, Cliniques Saint Eloi, 34000 Montpellier, France; or Prof. Dr. Med. H.-P. Heilmann, Hermann-Holthusen-Institut für Strahlentherapie, A.K. St. Georg, Lohmühlenstrasse 5, Federal Republic of Germany.

SOCIETY FOR RADIOLOGICAL PROTECTION

THIRD INTERNATIONAL SYMPOSIUM—INVERNESS 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ. Abstracts to be received by July 15, 1981.

3RD WORLD FEDERATION MEETING FOR ULTRASOUND IN MEDICINE AND BIOLOGY: JULY 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01-486 6582).

3RD WORLD CONGRESS OF NUCLEAR MEDICINE AND BIOLOGY

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

WORLD CONGRESS ON MEDICAL PHYSICS AND BIOMEDICAL ENGINEERING 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

5TH SOUTH AFRICAN INTERNATIONAL RADIOLOGICAL CONGRESS

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas sponsors, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

Book reviews

	Page
A textbook of radiology and imaging	565
Nuclear medicine examination review	585
Nuclear medicine: hepatolienal	585
Fast neutrons in the treatment of cancer	605
Cellular radiobiology	614
Known effects of low-level radiation exposure	625
Introduzione alla medicina nucleare	625
Investigative ultrasonology. 1	631
Optimization of radiotherapy	637
Draft British Standard	637

Clinical and Experimental Applications of Krypton 81m

Edited by J. P. Lavender

British Journal of Radiology, Special Report 15.
This work is composed of papers presented at an International Meeting held in June 1977 concerned with a new physiological tool; the use of a very short-lived radioactive gas krypton 81 m.
Krypton 81 m is a noble gas with a 13 second half life available from a portable generator with a half life of 4½ hours. Although known for a number of years it has only been used with any frequency by physiologists and clinicians since 1975.
The first section of the book deals with the production of the parent isotope rubidium 81 and the design of generators. The second section comprises a series of papers concerned with the use of the equilibrium image as both a picture and a measure of regional lung ventilation and perfusion. It also outlines problems of deriving absolute values of lung function. In the third section, papers illustrate the use of krypton 81 m as a clinical tool in the diagnosis of pulmonary embolic disease and other pulmonary diseases and compare such information with that obtained from the more familiar xenon 133. In the last section the use of intra-arterial krypton as a marker of regional myocardial and cerebral blood flow is discussed. This technique, which has been most highly developed in the case of the myocardium, allows detailed images of the myocardial perfusion to be recorded. Perhaps its clearest application is in following rapid changes of regional myocardial perfusion in response to transient ischaemia, stress and drugs.
The discussion following each paper allows an assessment of the value and place of this new technique.
ISBN 0 905749 01 4
ISSN 0306–2120 Price **£12**
Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237) or through your bookseller.

VOL 54 NO 643 JULY 1981

The British Journal of Radiology

Contents

Page

Diagnostic puncture in renal cystic dysplasia (multicystic kidney). Evidence on the aetiology of the cysts. 555
H. M. Saxton, S. J. Golding, C. Chantler and G. D. Haycock

The radiology of Meconium Ileus Equivalent. 562
D. W. Pilling and G. M. Steiner

The reliability of radiology in detecting prolactin-secreting pituitary microadenomas. 566
E. Teasdale, P. Macpherson and G. Teasdale

Vascular anatomy in the suboccipital region and lateral cervical puncture. 572
T. C. S. Cox, J. M. Stevens and B. E. Kendall

Clinical applications of radionuclide lung scanning in infants and children. 576
I. Gordon, P. Helms and F. Fazio

Radionuclide section scanning of the lungs in pulmonary embolism. 586
O. Khan, P. J. Ell, P. H. Jarritt, I. Cullum and E. S. Williams

Effects of acute administration of ethane hydroxydiphosphonate (EHDP) on skeletal scintigraphy with technetium-99m methylene diphosphonic acid (Tc-MDP) in the rat. 592
Iain Watt and Penny Hill

Cell labelling and cell damage with indium-111 acetylacetone—an alternative to indium 111 oxine. 597
Heather J Danpure and Safiye Osnan

Induction of spinal cord paralysis by negative pi-mesons. 602
H. I. Amols and J. M. Yuhas

Negative pion depth-dose profile examined by means of HeLa cell-survival curves. 606
D. H. Reading, M. A. Hynes, W. S. Spinks and A. H. W. Nias

The effects of NMR exposure on living organisms. I. A microbial assay. 615
A. Thomas and P. G. Morris

The effects of NMR exposure on living organisms. II. A genetic study of human lymphocytes. 622
P. Cooke and P. G. Morris

The iodine concentration in benign and malignant thyroid nodules measured by X-ray fluorescence. 626
T. G. Tadros, M. N. Maisey, S. C. Ng Tang Fui and P. C. Turner

Technical note. 630
A water bath for thyroid scanning with ultrasound.
L. A. Berger, A. Lister and A. C. Lilley

Case reports. 632
Vocal cord paralysis after treatment of thyrotoxicosis with radioiodine.
A. M. Robson
Antenatal diagnosis of duodenal atresia.
P. Farrant, K. C. Dewbury and H. B. Meire

Short Communication. 636
Simplified cell labelling with indium-111 acetylacetonate and indium-111 oxinate.
W. Th. Goedemans

Correspondence. 638
The oncogenic potential of X rays and/or hyperthermia in C3H-10T$\frac{1}{2}$ cells.
G. P. Raaphorst, E. I. Azzam, M. D. Sargent, M. Einspenner and J. Borsa
Whither the röntgen?
B. Stedeford and A. Dixon-Brown

Analysis of publications, 1978, 1979 and 1980. 640

Forthcoming events. 641

(*For book reviews see inside back cover*)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16647

14.9.82

August 198

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis

Radiation oncology

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

and related [illegible]

Published b
The British Institute of Radiolog

The British Journal of Radiology

Founded 1896

The Editorial Committee consists of:

The Editors:

D. K. Bewley, M.A., PH.D. J. Roylance, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. Hale, M.B., CH.B., F.R.C.R., D.M.R.T. J. L. Haybittle, M.A., PH.D.,
A. B. Ayers, M.D., D.M.R.D., F.R.C.R.

and

The Associate Editors:

Thelma D. Bates, M.B., CH.B., F.R.C.R., D.C.R.A.
D. Cosgrove, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. Cottrall, B.A., M.SC., PH.D., F.INST.P.
J. C. W. Crawley, B.SC., C.ENG., M.I.E.E.
R. Dick, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. Flower, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. Gleeson, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. Gravelle, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. Keeling, M.A., M.SC., M.B.
I. Kelsey Fry, D.M., F.R.C.P., F.R.C.R.
B. Kendall, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. Meire, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
N. J. McNally, B.SC., M.SC., PH.D.
J. T. Patton, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. Perry, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. Savage, D.SC.
P. N. T. Wells, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. Armstrong, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. Cohen, PH.D., F.INST.P. (North America)
B. J. Cremin, F.R.C.R., F.R.A.C.R. (South Africa)
R. Fox, D.PHIL. (Australia)
H. A. Luke, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. Sim, M.B., F.R.C.R., M.R.C.A. (New Zealand)
D. M. Taylor, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: Mrs. L. F. Secretan, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

Advertisements: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01-836 5281).

Subscriptions: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

Annual Subscription: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
Patron: Her Majesty The Queen

Founded 1897
32 WELBECK STREET, LONDON W1M 7PG
Telephone: 01-935 6237 and 01-935 6867. Cable Address: "Britology, London W.1."

President: D. H. Trapnell, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries

M. F. Cottrall, B.A., M.SC., PH.D., F.INST.P.
H. B. Meire, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

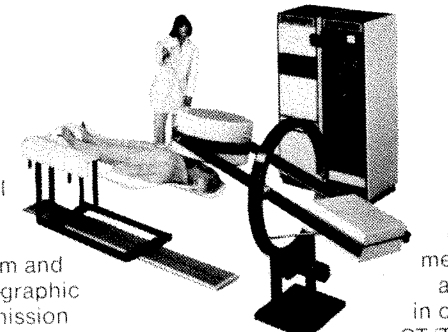
Hon. Treasurer: D. T. Kerrisk
General Secretary: Mrs. J. Royston

The British Institute of Radiology is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company offers a complete nuclear diagnostic ECAT system?

General Electric Company of U.S.A:*
Keeping you ahead of changing technology.



From one source — General Electric of U.S.A. — you can get both the MaxiCamera 400T nuclear camera system and a data processor with tomographic software for performing Emission Computed Tomography (ECAT) studies.

Because they were designed for each other — not acquired and put together from different suppliers — you get maximum performance from both: providing, for example, an added diagnostic dimension for visualising the liver, brain and heart.

Emphasis on advanced technology extends to other systems as well. In multi-axis vascular imaging, General Electric of U.S.A. combines the state-of-the-art Fluoricon L300 imaging system with fully compatible digital fluorography to meet growing diagnostic and therapeutic needs; in computed tomography, CT/T system technological advances include Dynapak expanded dynamic scanning, Arrange reformatting capability and nominal 1.5 mm slice thickness; in ultrasound, Datason system with real time sector scanning optimizes acoustic access for enhanced visualisation of anatomy.

Advanced imaging technology. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

Frankfurt/M. Tel. 06 11 7 60 73 69 • Wien Tel. 24 14 51 • Brüssel Tel. 660 2010 • Kopenhagen Tel. 2 86 86 00 • Mailand, Tel.: 753 1351 •
Breda, Tel. 76 22 54 15 • Lissabon, Tel.: 36 71 55 • Madrid, Tel.: 252 5100 • Goteborg, Tel.: 42 09 70 • Zurich, Tel.: 47 50 30

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

St. Laurence's Hospital
Richmond Whitworth & Hardwicke Hospitals
and Jervis Street Hospital

Applications are invited from qualified Medical Practitioners for the following wholetime post:

Consultant Radiologist
(with a special interest in Ultrasound)

Facilities within the Department include:
Angiography, Ultrasonography, CT Scanning and Nuclear Imaging.

Applicants must possess the following qualifications:

1. (a) the Fellowship of the Faculty of Radiology of the Royal College of Surgeons in Ireland or a qualification in radiology at least equivalent thereto, **or**
   (b) a recognized diploma in medical radiological diagnosis awarded before May 1966 or a qualification in radiology before May 1966 at least equivalent thereto, **and**
2. (a) in the case of persons who possess the qualifications at 1 (a) above the specialization, on a full time basis, in the practice of Radiology for at least five years, **or**
   (b) in the case of persons who possess the qualifications at 1 (b) above, the specialization, on a full time basis, in the practice of Radiology since acquiring such diploma.

Particulars of appointment may be obtained from the Secretary/Manager's Office, St. Laurence's Hospital, North Brunswick Street, Dublin 7, to which Curriculum Vitae (12 copies) must be sent, to arrive not later than 12.00 noon on Monday, August 31, 1981.

Royal Free Hospital/Fischer Ultrasound
Course in Medical Ultrasound

Introduction to all aspects of Diagnostic Ultrasound

Subjects to include:
Physics of Ultrasound
Equipment
Photographic aspects
Applied anatomy/physiology where required
Clinical applications to include Obstetrics/Gynaecology, General Abdominal, Cardiology, Ophthalmology, Orthopaedics, Paediatrics, Doppler, etc.

Practical training in most of the above clinical applications is given.

Venue – **Royal Free Hospital Schools of Radiography & Ultrasound and Departments of Clinical Ultrasound, Royal Free Hospital.**

Dates – **9 November to 20 November** (excluding weekends).

For further details and Application Form please contact:

Fischer Ultrasound Course,
c/o Mr. W. Smith, Royal Free Hospital
School of Ultrasound,
17 Lyndhurst Gardens, London NW3.

Specialist: Dept. of Radiology

for a 3-year contract post in Cape Town, South Africa, one of the world's most attractive coastal cities.

This vacancy exists within the Provincial Administration of the Cape of Good Hope's Hospitals Department at the Red Cross War Memorial Children's Hospital in Rondebosch, Cape Town.
On the joint staff of the Red Cross War Memorial Children's Hospital/University of Cape Town, this post offers excellent opportunities for further training in Paediatric Radiology as well as a wide range of Pathology. Previous experience is not essential.
The salary is R22,650 (fixed) per annum and R1 is equal to £1 in purchasing power.
In addition to the salary indicated and subject to compliance with certain conditions, the successful applicant will be entitled to an annual service bonus of ± one month's salary, medical aid scheme and generous holiday and sick leave privileges.
On acceptance of a three-year contract, certain transportation costs will be covered. If a three-year contract is not agreed to, the Department of Immigration at the South African Embassy in London may be approached for financial assistance.

For further information, contact Professor B. J. Cremin or the Medical Superintendent at the Red Cross War Memorial Children's Hospital, Rondebosch, 7700, Cape, Republic of South Africa.

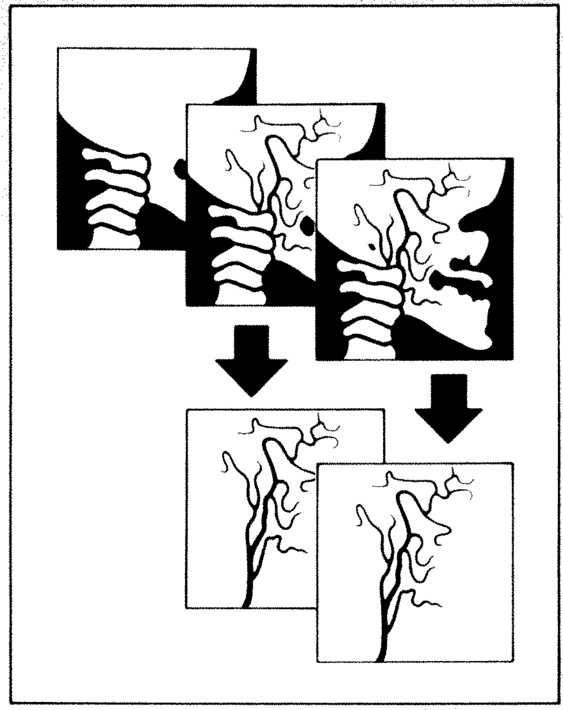
IT'S YOUR RESULTS THAT MATTER.

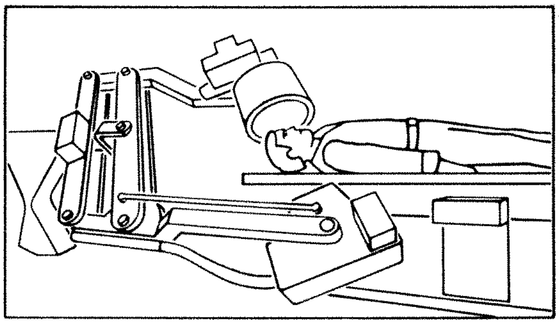
Digital vascular imaging.

DVI is an advanced digital processing system for performing intravenous angiography with real-time image subtraction.

DVI provides angiographic-calibre information achieved by IV contrast administration and is

- relatively non-invasive
- a low risk technique
- quick and simple
- easy to perform:
  - ○ no catheter manipulation
  - ○ no sterile technique
  - ○ no femoral puncture or cutdown
  - ○ no post-procedure patient monitoring
- an ideal outpatient procedure requiring no hospitalisation
- cost effective





DVI's clinical applications include:

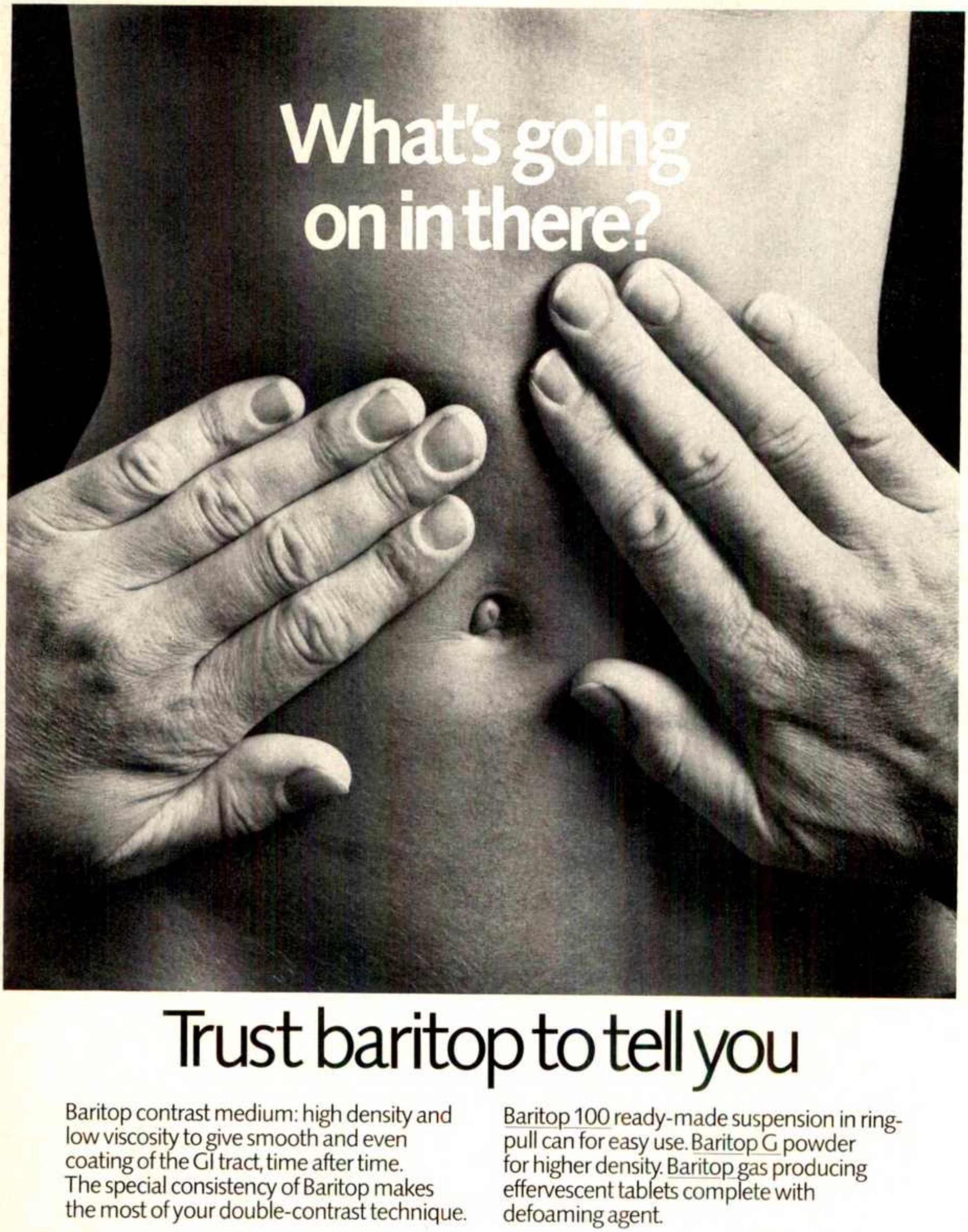
- asymptomatic vascular disease screening
- evaluation of the high risk patient
- post-surgical evaluation and follow up
- an adjunct to both conventional and interventional angiography
- a "first order" diagnostic tool in lieu of conventional angiography

Because of DVI's unique subtraction and enhancement capabilities, other potential applications most certainly will develop with increased clinical usage.

PHILIPS

Medical Systems

For detailed information write to Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 0LJ.



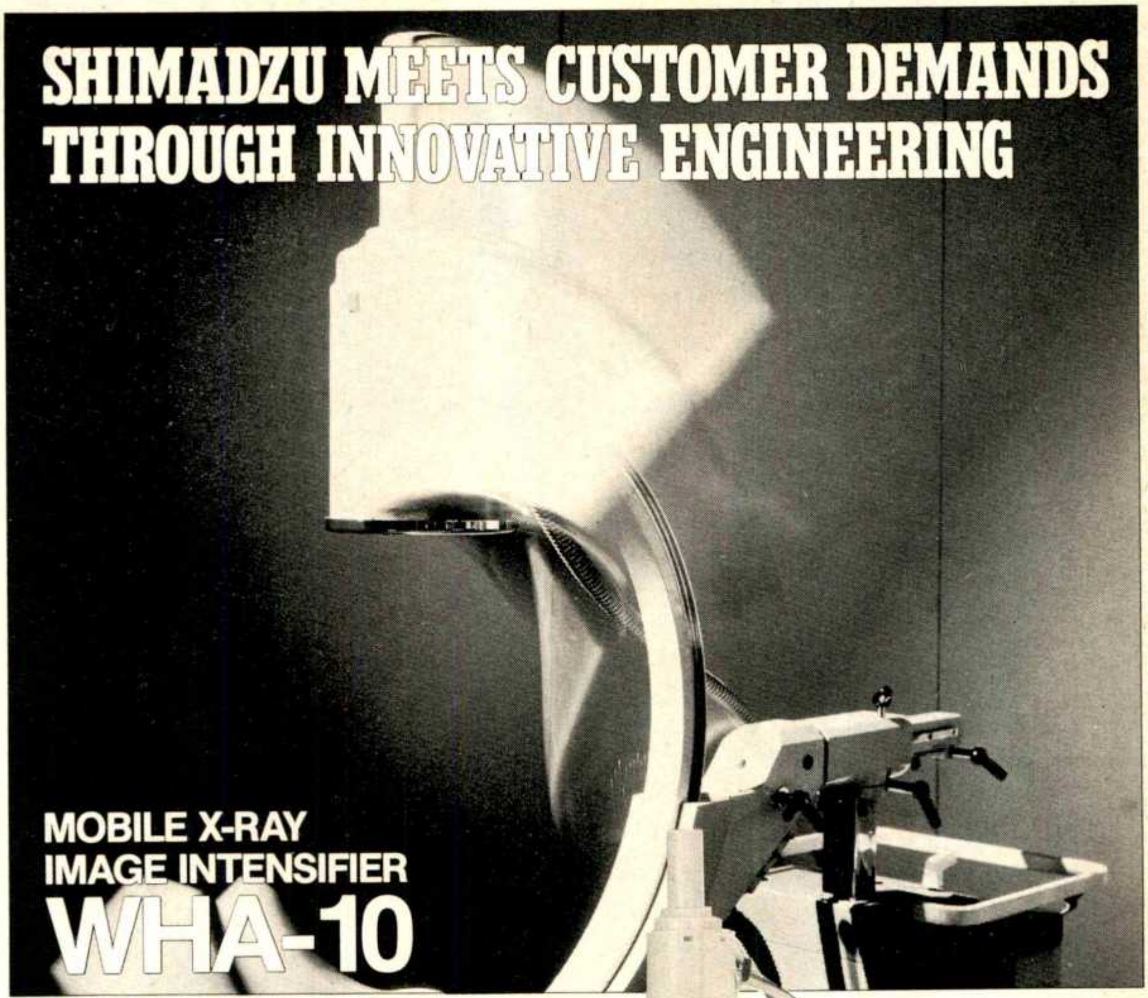
Trust baritop to tell you

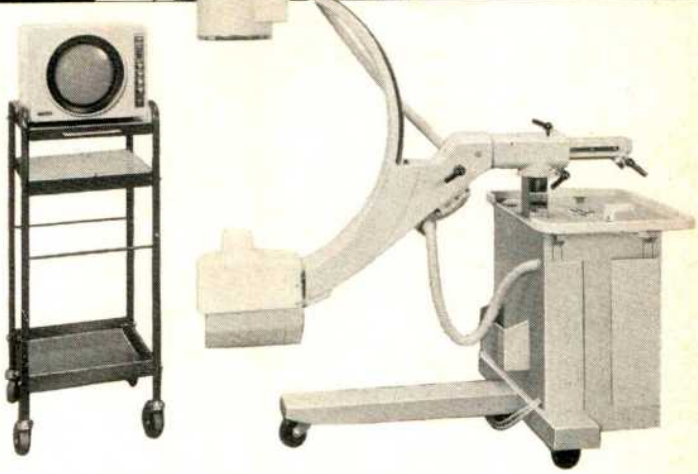
Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.


SHIMADZU MEETS CUSTOMER DEMANDS
THROUGH INNOVATIVE ENGINEERING
MOBILE X-RAY
IMAGE INTENSIFIER
WHA-10



High quality image ....
- 0.4mm focus x-ray tube
- Image Brightness Stabilizer

High output ....
- Square full-wave rectification x-ray generator

Less x-ray radiation ....
- Video memory
- Motor driven collimator

Simple operation ....
- Radiographic condition memory (Optional)

Free access to patient ....
- Large C-arm steering handle

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D.
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

RADIATION ONCOLOGY
CROSS CANCER INSTITUTE
EDMONTON, ALBERTA

Applications are invited for the position of radiation oncologist in the Cross Cancer Institute. There are at present ten radiation oncologists, five residents in training and a team of assistant physicians. The in-patient service comprises 76 beds and the equipment includes a 20 MeV and two 6 MeV linear accelerators, Cobalt and Superficial X-ray units, simulator, full mould room facilities, fully computerized treatment planning and whole body CT scanner. Over 2,000 patients receive radiotherapy each year. Research into new treatment modalities is well funded in both the clinical and laboratory areas of radiation oncology, radiobiology and medical physics. The Institute has departments of Medicine, Surgery, Gynaecology, Pathology, Diagnostic Radiology, Nuclear Medicine, Medical Physics and Radiobiology devoted to oncology; it is sited on the University campus, affiliated to the University of Alberta Hospital, and it is a referral and research center for the whole spectrum of malignant disease in a rapidly growing population which is now one million two hundred thousand. Remuneration according to qualifications and experience.

For more information please contact:

Dr. James G. Pearson, Director, Radiation Oncology, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta Canada, T6G 1Z2

Telephone: (403) 432–8755

16-18 September 1981
London

Conference and
Trade Exhibition

Paediatric Cardiology
1981

Organising Committee:
Prof. R. H. Anderson, Dr. E. A. Shinebourne,
Prof. F. J. Macartney, Dr. M. Tynan.

Sponsored by the British Heart Foundation
Speakers will include: S. Howarth, A. Pacifico,
M. Paul, J. Somerville, M. Yacoub, A. Becker,
O. Scott, D. Heath, M. Godman, J. Taylor, D. Southall,
D. Krickler, D. Ward, G. Thiene, J. Stark,
A. Carpentier, J. Wilkinson, J. Lincoln,
E. Gussenhoven, L. Allan, D. Gibson, G. Miller,
P. Deverall, S. Hunter, M. Quero Jimenez, E. Silove,
M. de Leval, A. Bentovim, D. Silverman, N. Dennis,
A. Blancquaert, B. Keeton.

A reduced fee is available for Nurses and Radiology Technicians.

For further information:
Conference Services Ltd., 3 Bute Street,
London SW7 3EY, UK.
Tel: 01–584 4226. Telex: 916054 JOYBRI.

Computerized Tomographic Scanners in Radiotherapy in Europe

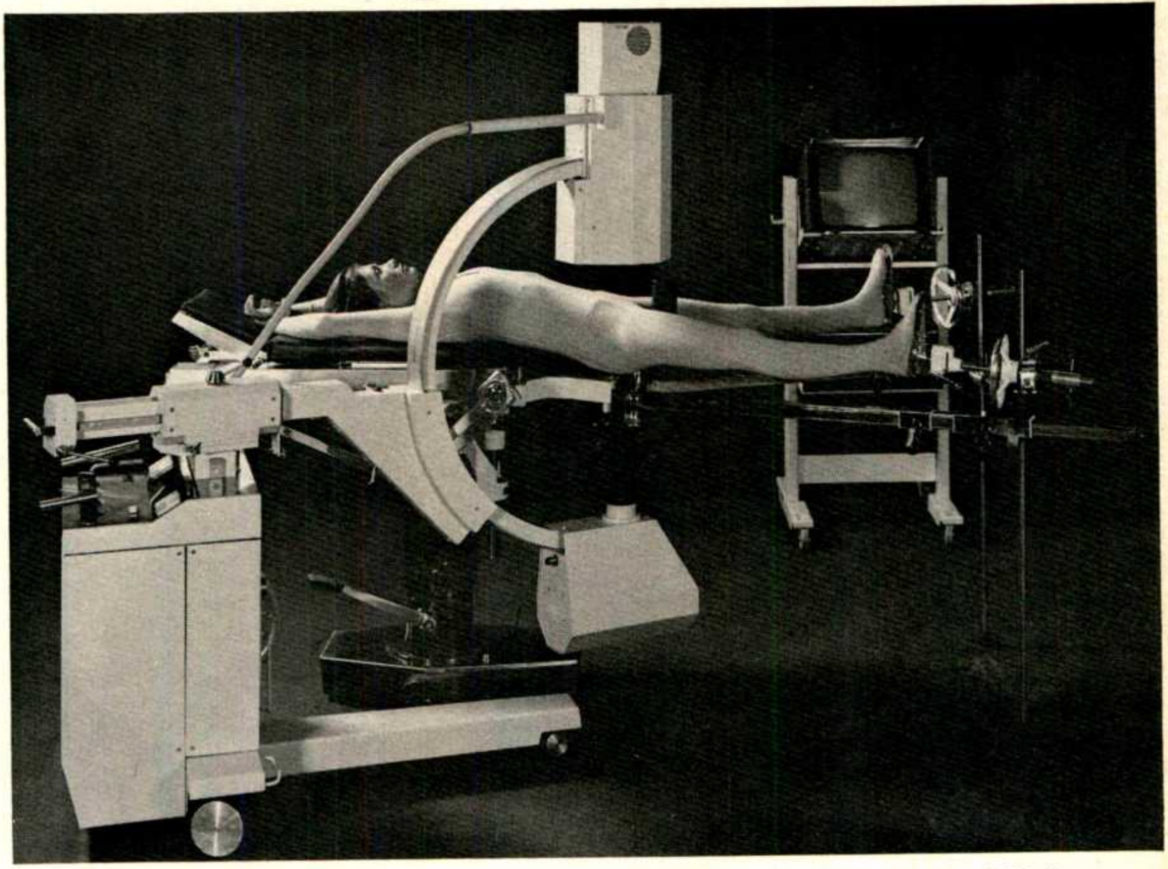
Edited by Roger J. Berry

British Journal of Radiology
Supplement 15

Under the auspices of the Commission Informatique of the European Association of Radiology, a Workshop was held at the Headquarters of WHO, Geneva, from 28 to 30 March 1979 on 'The Use of Computerized Tomographic Scanners in Radiotherapy in Europe'. It was clear from the first that CT scanning would have a major impact on radiotherapy, but how and where? At this meeting 150 experts from 17 countries met to review, from a real background in clinical experience of using CT scanners in radiotherapy planning, the progress which had been made and the costs involved. CT scanning is not inexpensive, but the information provided is in many cases unique. Following a keynote address by Professor Brian Pullan of the University of Manchester outlining what is and is not likely to be possible in future in tumour imaging, the papers cover the practical use of CT scan information in assessing tumour volume, planning radiotherapy and following tumour response in the head and neck, the thorax and the abdomen. The linkage of CT information to radiotherapy treatment planning is discussed, and the way indicated towards true three-dimensional radiotherapy planning. All the papers presented at the Meeting are included in abridged form as well as rapporteurs' reports of the discussions in each section.

Orders to:
Publications, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG
Price £19·50
ISBN 0 905749 09 X
ISSN 0007 1285

A rapid and precise surgical X-ray system with high-resolution TV



The streamline design for the CGR Optascop increases the range of applications in surgical radiology. Easier manipulation and greater mobility by steering castors allow precise positioning from the simplified control panel.

A complete mobile high-definition intensifier unit equipped with a TV camera and separate trolley-mounted monitor.

The dual focus x-ray tube with remote controlled collimator provides for radiography and fluoroscopy up to 100kV. The x-ray tube – intensifier TV movements are motor driven.

Optional extras are dose reduction pulsed fluoroscopy, and taped memory facility.

OPTASCOP
from

Full details and specification from
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166

Branches at: Bristol, Cambridge, Edinburgh,
Glasgow, Manchester, Nottingham

SIEMENS

When programmed x-ray diagnosis is preferred, we have the ideal combination

The multipurpose Siregraph C automatic x-ray table has enhanced routine diagnostic capability, including aniography of the body trunk and lower extremities.

The escutcheon of the Tridoros 712 MP generator puts all the radiographic parameters at your fingertips by means of microprocessor technology.

Programmed radiographic factors may be inserted by the Superintendent Radiographer or Radiologist and these factors are retained permanently under lock and key. This 70kW 12 pulse machine maintains high voltage accuracy yet offers extreme flexibility with provision for 49 programmes each for radiography and planigraphy.

For full details contact: Siemens Medical Group,
Siemens Limited, Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS. Telephone: (09327) 85691.

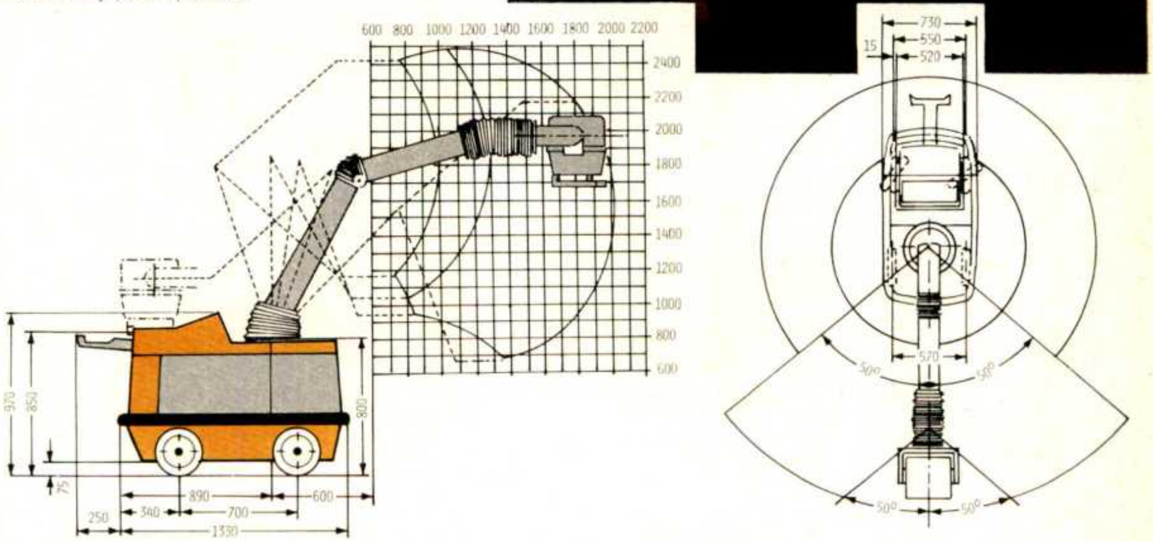
Siemens–the ultimate in cost effective x-ray diagnosis

SIEMENS

Mobil XR – brings a microprocessor controlled, aseptic mobile radiography unit to the patient.

The battery-powered MOBIL XR is self-propelled and self-contained with microprocessor controls providing full power exposures at 20 kW time after time. The adjustable counter-balance arm and a wide range of alphanumerically displayed exposure parameters allow sharp image examination of any organ or limb. Aseptic design with touch controls and total enclosure fo all components make it ideal for theatre use. Infinitely variable speed control makes it easy to manoeuvre and pull-out cable allows simple recharging at any power point.

For further details or a demonstration contact:
Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS.
Tel. Sunbury (09327) 85691.



In the world of mobile radiography Siemens has the answer.

Royal Perth Hospital

RADIOLOGISTS

Applications are invited for two full-time consultant positions.

These positions have become available as a result of the broadening of the range of services offered through the acquisition of new equipment, including a Seimens whole body C.T. Scanner.

One position requires C.T. Scanner and Ultrasound expertise and the other requires expertise in Angiography. It is desirable that applicants for the latter position have also had some experience in C.T. and Ultrasound. Both appointees will be required to carry out other general Radiological duties within the Department and also participate in the "ON CALL" roster.

There are currently 6 full-time and 9 part-time Radiologists working in the Department. Royal Perth Hospital (1072 beds) is the largest acute general hospital in the State and the largest teaching hospital associated with the University of Western Australia. Several regional specialist units are included within it. The Department of Diagnostic Radiology is a large one (18 rooms) undertaking a wide range of investigations. The duties of Radiologists include medical student and registrar training. A Departmental Trust Fund provides financial assistance for research and post graduate study.

QUALIFICATIONS: Medical Practitioners registerable within the State of Western Australia, with appropriate higher radiological qualification.

REMUNERATION: Full details will be supplied on application to Dr. T. M. Chakera (Head of the Department of Diagnostic Radiology).

CONDITIONS OF SERVICE: In accordance with the "Metropolitan Teaching Hospitals Salaries and Conditions of Service Agreement 1979 — Clinical Staffs".

FURTHER INFORMATION: A Memorandum of information is available on request.

APPLICATIONS: To be addressed to the Administrator, Royal Perth Hospital, Box X2213, G.P.O., Perth, Western Australia, 6001, and to include personal details, age, qualifications, experience, publications, names and addresses of two referees, recent photograph.

CLOSING DATE: Friday, September 4th, 1981.

Senior posts at Groote Schuur Hospital in Cape Town

The Hospitals Department of the Provincial Administration of the Cape of Good Hope has the following vacancies at the Groote Schuur Hospital In Observatory, Cape Town, probably the world's most attractive coastal city.

PRINCIPAL SPECIALIST

Salary: R26,250 (fixed) per annum (£1 sterling equals R1.79).

PRINCIPAL PROFESSIONAL OFFICER (Radiobiologist)

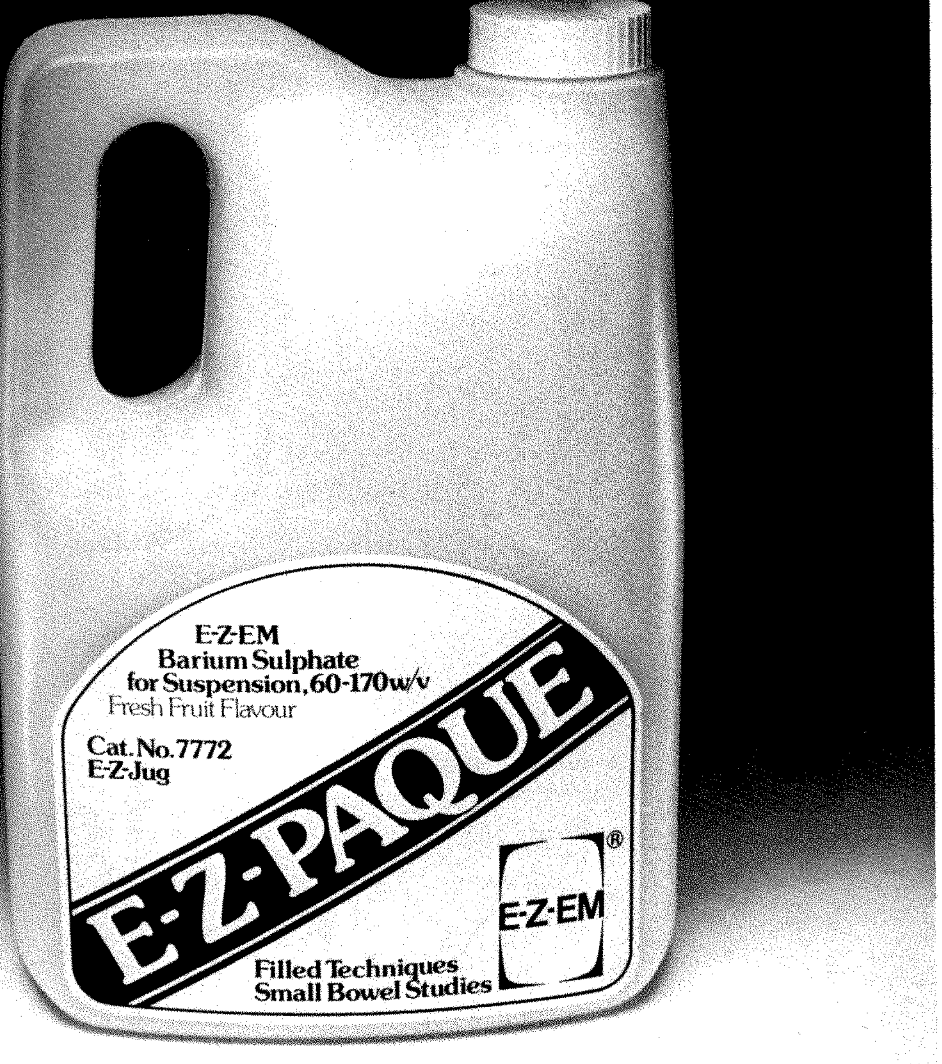
Salary: R15,870×735–R19,545 per annum (£1 sterling equals R1.79).

Both posts are on the Joint Staff of the Cape Provincial Administration at the Groote Schuur Hospital and the University of Cape Town, and will carry Senior Lecturer status. The Radiotherapy Department at Groote Schuur Hospital is a major department which, along with two sub-departments, sees over 5,000 new cancer patients per annum. Duties will be to assist the Head of the Radio-Therapy Department to develop these facilities, which are to be developed jointly with another teaching hospital in the Western Cape.

A large cyclotron is being built at Faure, about 12 miles from Groote Schuur Hospital, by the Council for Scientific and Industrial Research. This machine would have facilities for proton therapy up to 200 MeV, neutron therapy at about 25 MeV and Helium-3 up to about 300 MeV and will be operational in 1984. At the present time the design and development of the treatment facility is under way. Considerable radiobiological facilities will be available for cell, small- and large animal studies, and extensive facilities provided for clinical radiobiological studies and clinical trials.

Further details and application forms are obtainable from the Medical Superintendent, Groote Schuur Hospital, Observatory 7925, Cape Town, Republic of South Africa.

E-Z-Jug...



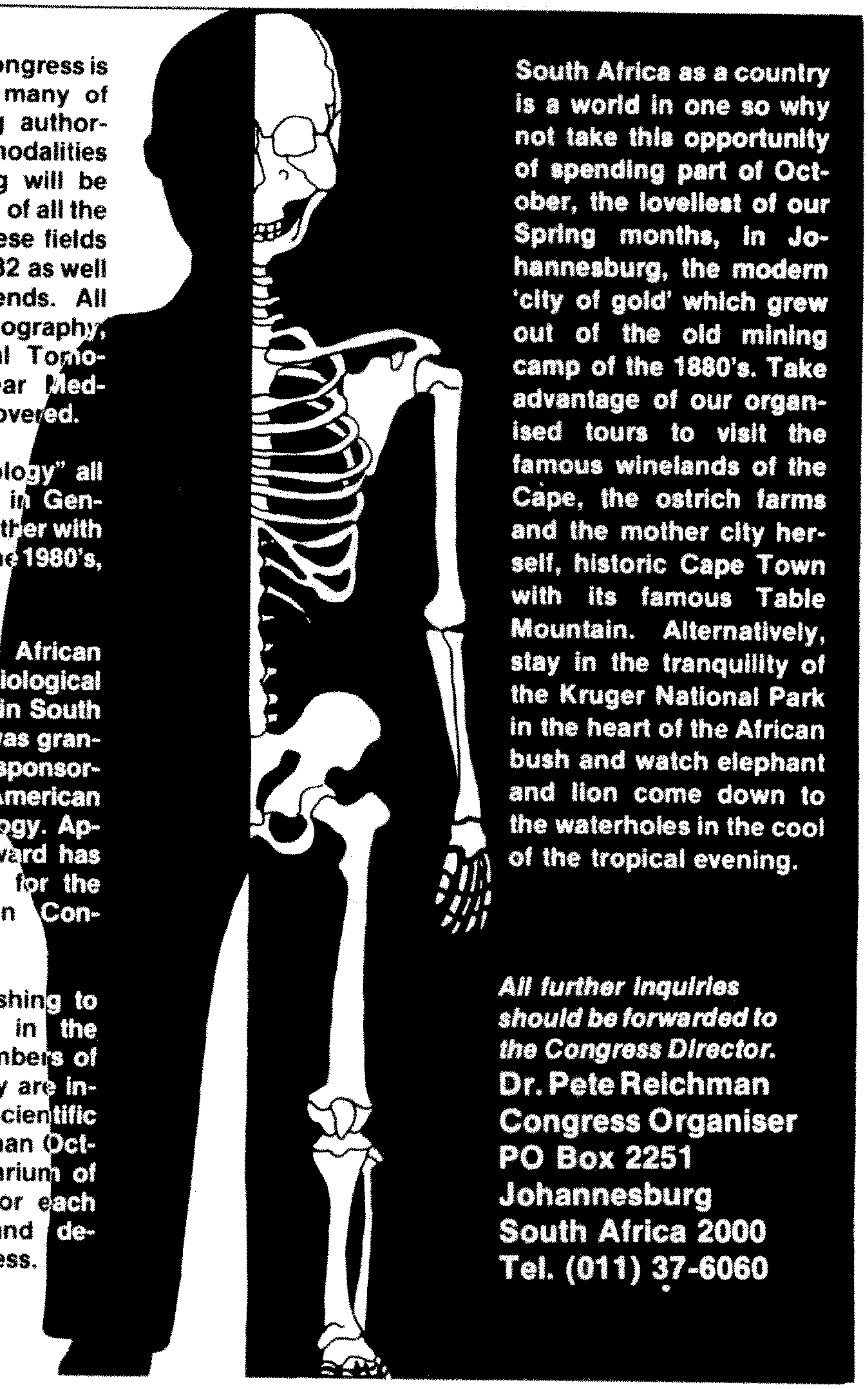
Also available Cat. No. 750 unit dose cups and Cat. No. 747 10kg bulk packs.

E-Z-EM®

Full details from:
Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151
Produced by E-Z-EM Ltd London

PL/1665/0002

FIFTH SOUTH AFRICAN INTERNATIONAL RADIOLOGICAL CONGRESS
"IMAGEOLOGY 1982"
OCTOBER 8 — 15TH 1982.



The theme of the Congress is "Imageology" and many of the world's leading authorities in the various modalities of medical imaging will be giving detailed talks of all the developments in these fields prior to October 1982 as well as their future trends. All aspects of Ultrasonography, Computerised Axial Tomography and Nuclear Medicine will be fully covered.

Apart from "Imageology" all the latest advances in General Radiology, together with its future course in the 1980's, will be discussed.

The Fourth South African International Radiological Congress was held in South Africa in 1978 and was granted a Credit 1 co-sponsorship by the American College of Radiology. Application for this award has already been made for the Fifth South African Congress in 1982.

Those delegates wishing to participate actively in the programme as members of the Overseas Faculty are invited to submit scientific papers by no later than October 1981. An Honarium of $250 will be paid for each lecture accepted and delivered at the Congress.

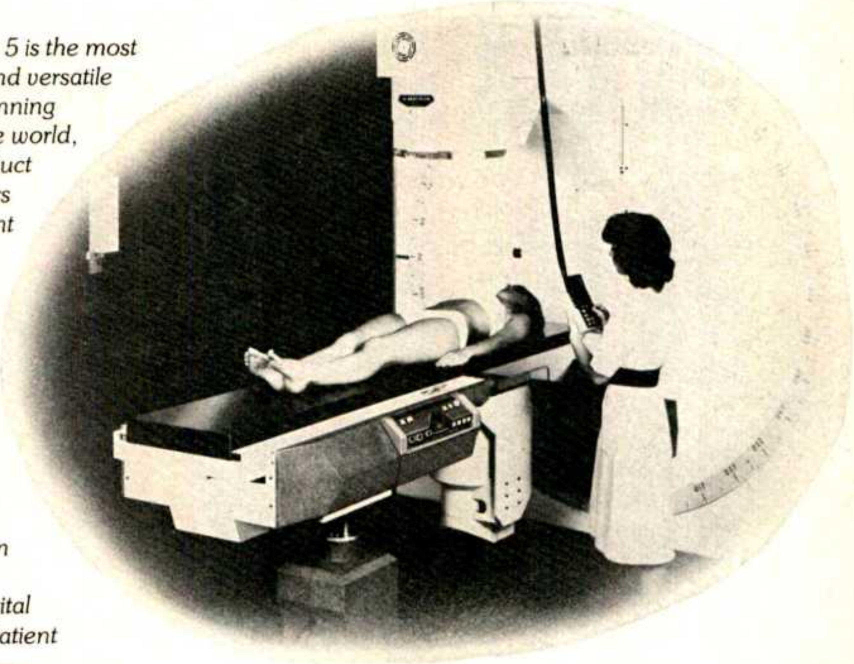
South Africa as a country is a world in one so why not take this opportunity of spending part of October, the loveliest of our Spring months, in Johannesburg, the modern 'city of gold' which grew out of the old mining camp of the 1880's. Take advantage of our organised tours to visit the famous winelands of the Cape, the ostrich farms and the mother city herself, historic Cape Town with its famous Table Mountain. Alternatively, stay in the tranquility of the Kruger National Park in the heart of the African bush and watch elephant and lion come down to the waterholes in the cool of the tropical evening.

All further inquiries should be forwarded to the Congress Director.

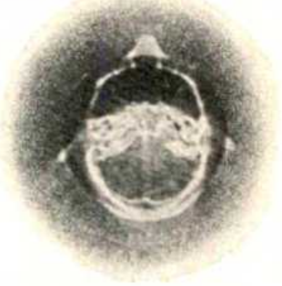
Dr. Pete Reichman
Congress Organiser
PO Box 2251
Johannesburg
South Africa 2000
Tel. (011) 37-6060

Ximatron 5 Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

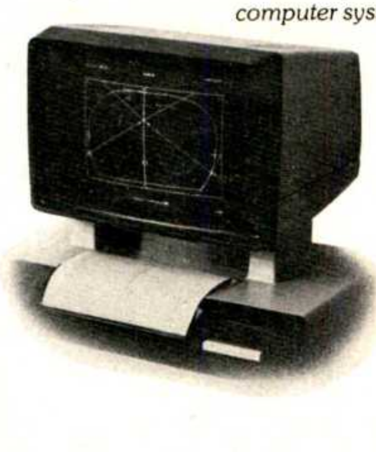


Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY

Nuclear Medicine Communications

INTERNATIONAL RAPID PUBLICATION

EDITORS:

K.E. Britton, London;
P.J. Ell, Bern;
R.F. Jewkes, London

ADVISORY EDITORS

(US and Canada):
M. Donald Blaufox; A.B. Brill; D. Gilday; G.T. Krishnamurthy; R.M. Lambrecht; B.J. McNeil; E.L. Nickoloff; N.G. Nolan; S.M. Pizer; M.L. Thakur; R.A. Vogel; H. Wagner plus international authorities from many other countries

- * **Provides an English language forum for original papers of high quality**
- * **Allows rapid communication of new research**
- * **Includes conference reports and newsletter material**
- * **Published in association with** The British Nuclear Medicine Society

1981 Subscription Details:

Six issues per year
384 pages per volume (6 issues)
First published March 1980
UK: £24 per annum
Overseas: £27.50 per annum
Single copies: £5.00
ISSN: 0143-3636

SPECIMEN COPIES

For further information or a **specimen issue** please write to:
Promotional Department
Chapman and Hall Ltd
11 New Fetter Lane
London EC4P 4EE

RADIATION PROTECTION of the PATIENT

A Manual of Good Practice

Edited by : Walter A. Langmead

Part I. — Diagnostic Radiology

Price £2.95

This Manual is concerned with the radiation protection of patients undergoing diagnostic examinations or treatment with ionising radiations. It examines the responsibilities of the many individuals – general practitioners, clinicians, radiologists, radiographers and physicists – whose special fields of knowledge together contribute to the radiation safety of the patient, and it proffers advice to each in turn as to the preferred procedures to minimise the patient's radiation dose without reducing the level of diagnostic achievement or the efficacy of treatment.

The Manual is to be published in two Parts, dealing with radiology and with nuclear medicine and radiotherapy. PART I. – DIAGNOSTIC RADIOLOGY, covers the X-ray examination from the initial request to the final report. The scientific and technical factors which enable the clinical objectives to be attained with minimal dose to the patient are also reviewed. Two Appendices give recommendations respectively for certain specialised X-ray examinations, and for a departmental guide to radiographic procedures.

The benefits of medical diagnosis and treatment with radiation are large and the potential radiation hazards arising therefrom are comparatively minor in most cases. Nevertheless, the safety of the patient is paramount and this results from good teamwork and attention to detail, as outlined in this Manual.

Prepared by Panels of the British Radiological Protection Association; and published by The British Institute of Radiology.

Orders to BIR Publications, 32 Welbeck Street, London W1M 7PG (01–935 6867)

British Council Medical Courses

Medical Oncology in the 1980s. The Co-ordinated Approach

14–26 March 1982 in London

The intention of this course is to focus on the main new areas of basic research and clinical techniques which may improve the current management of various tumours. The course will include a brief review of our current understanding of abnormalities in the tumour cell, improvements in diagnostic and tumour localising techniques, the development of new anti-cancer drugs, the application of tumour markers and their application in management of various tumours and a detailed discussion of the application of chemotherapy in common, and some of the uncommon, forms of human cancer. The course will be arranged at the Postgraduate Medical Centre at the Charing Cross Hospital, London. The Director of Studies is Professor K D Bagshawe. This course is intended for medical oncologists, radiotherapists and senior clinicians with a major interest in oncology.
There are vacancies for 30 members.
Fee including demi-pension accommodation £575.
Applications must be received in London by 15 November 1981.

The Biological Basis of Radiotherapy

7–19 February 1982 in London

The course will be directed by Professor G E Adams and Professor M J Peckham of the Institute of Cancer Research and Royal Marsden Hospital. Examples of the subjects which will be covered are: molecular, cellular and tissue radiobiology, including mechanisms of radiation action and cellular response, modification of radiation effects by oxygen, chemical radiation sensitisers, radioprotective drugs, cytotoxic drugs, hyperthermia, radiation quality dose-rate and fractionation.
This course is intended for Professors and Heads of departments of Radiotherapy and Radiobiology, clinicians with a major interest in radiation oncology, pharmacologists working with radio sensitisers and chemotherapy.
There are vacancies for 40 members.
Fee £590
Applications must be received in London by 21 September 1981.

Urological Cancer

18–29 April 1982 in London

The aim of this course is to review modern concepts and results in the epidemiology, diagnosis and treatment of cancer of the urological system. It is intended to appeal to both the clinician and the research worker and in a decade which has seen rapid advances in laboratory and hospital to give each a better understanding of the problems and objectives of the other in their respective fields. The joint Directors of Studies will be Professor J P Blandy of The London Hospital and Dr R T D Oliver of the Institute of Urology, London. The working sessions of the course will take place at The London Hospital Medical College.
There are vacancies for 30 members.
Fee including demi-pension accommodation £630.
Applications must be received in London by 31 December 1981.

Application forms and further information can be obtained from local overseas Representatives of the British Council or from The Director, Courses Department, 65 Davies Street, London W1Y 2AA Britain.

WE'RE OLD FASHIONED

Old fashioned letter headings which actually show the exact nature of our business which is the supply of X-ray accessories, and has been since 1910.

Old fashioned invoices written in old fashioned prose.

Old fashioned courtesy in replying promptly to correspondence, however trivial.

Old fashioned direct-line telephones to executives.

Old fashioned standards of working until the job is done.

Old fashioned offices with a Preservation Order, cosy adjustable gas-fires and wall-to-wall carpets.

Old fashioned flower garden with a wrought-iron gate to the church-yard (yes, we know this one leaves us wide open to wise-cracks).

Old fashioned warehouse in a range of cottages in Cow Lane.

If you like concrete structures, computers, switchboards who leave you in the air, minimum-order conditions and all the other ideas adopted by progressive firms, we are not for you—but you'd be surprised to know how many thousands of people seem to be old-fashioned enough to deal with a firm like us.

EVERYTHING X-RAY

since **1910**

CUTHBERT ANDREWS

EVERYTHING X-RAY LTD.

5 HIGH STREET, BUSHEY VILLAGE, WATFORD WD2 1BE

Overseas telegrams:
EXRAYZE WATFORD

Telex:
Evex 925859
Elwood G

Telephone:
01-950 2525

1981, *British Journal of Radiology*, 54, 643–650
VOLUME 54 NUMBER 644 AUGUST 1981

The British Journal of Radiology

Round (helical) atelectasis

By *S.-R. Cho, M.D., *D. A. Henry, M.D., *M. C. Beachley, M.D. and †J. W. Brooks, M.D.

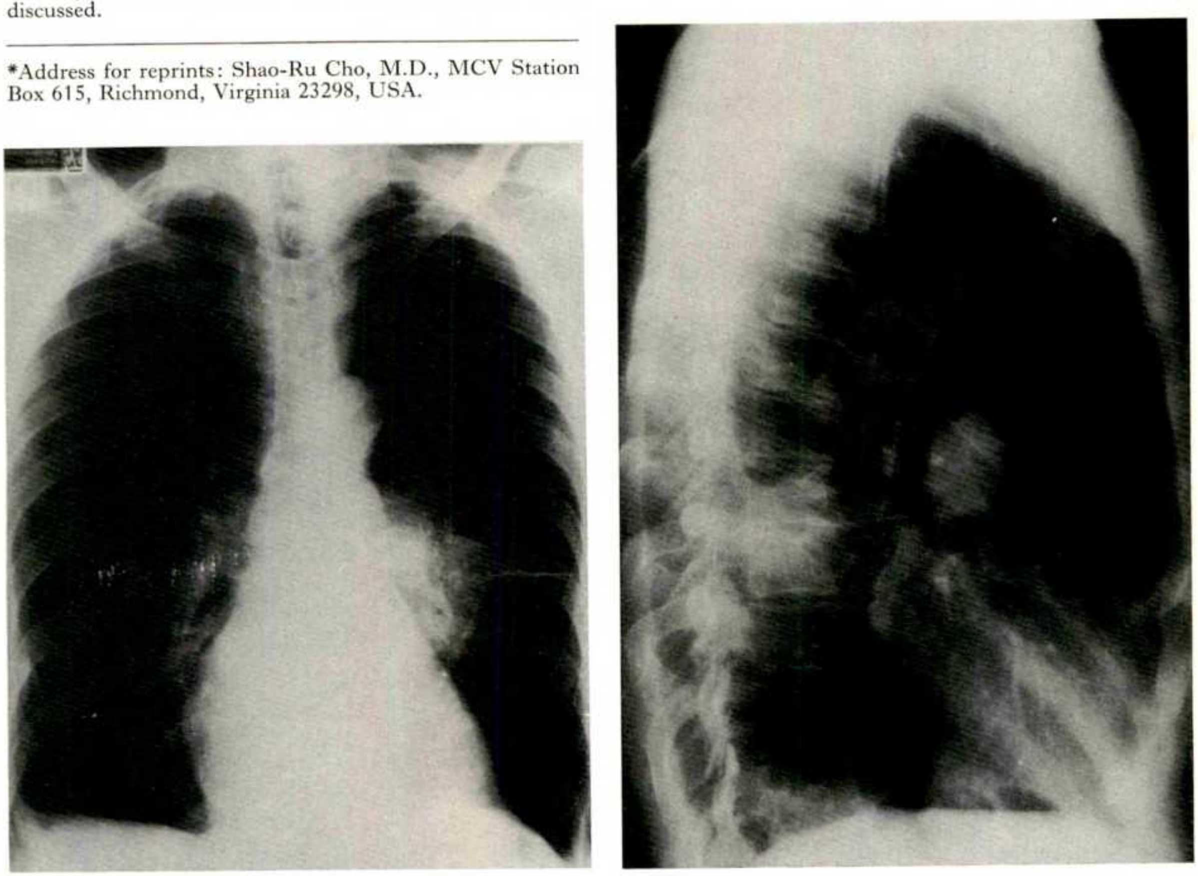
Departments of *Radiology and †Surgery, Virginia Commonwealth University/Medical College of Virginia, Richmond, Virginia, USA

(*Received October 1980 and in revised form March 1981*)

ABSTRACT

Round (helical) atelectasis is a little-known form of pulmonary collapse. It is thought to occur secondary to lung compression from pleural effusion or following therapeutic pneumothorax. Its occurrence is favoured in patients with exudative pleural effusions and extensive pleural thickening. It presents radiographically as a pulmonary pseudotumour, and experience with this entity and its pathogenesis are discussed.

Round atelectasis (RA) is an unusual, localized form of lung collapse which has only recently been discussed in the English literature (Schneider *et al.*, 1980; Hanke and Kretzschmar, 1980). These coiled, mass-like lesions are seldom truly round and the



A FIG. 1. B

(A) PA and (B) lateral views of the chest demonstrate a 4 cm mass in the superior segment of the left lower lobe. Over-expansion of the left upper lobe with downward displacement of the left hilum is seen. There is blunting of the costophrenic angles due to previous pleural disease.

---

*Address for reprints: Shao-Ru Cho, M.D., MCV Station Box 615, Richmond, Virginia 23298, USA.

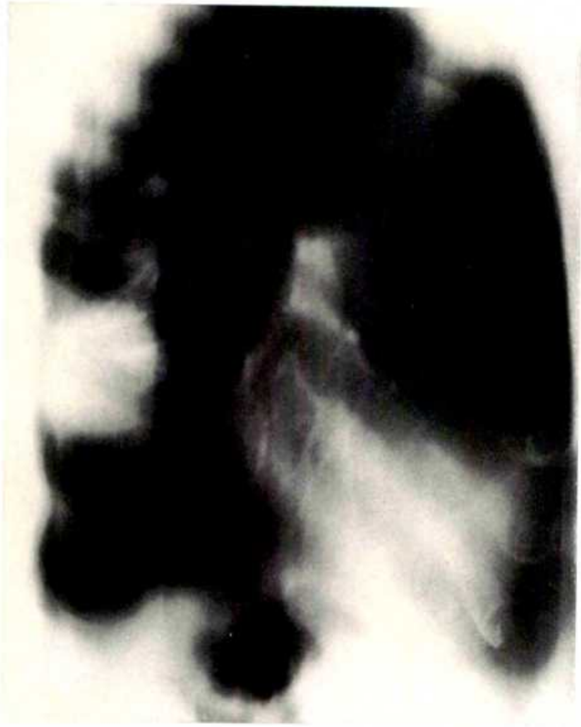


Fig. 1c.

A tomogram, lateral cut, at the peripheral portion of the mass shows numerous linear stripes radiating from the mass toward the posterior pleura.

term "helical atelectasis" is more descriptive and recalls their pathogenesis. However, in the interest of avoiding confusion, the term "round atelectasis" will be used. RA presents radiographically as a rounded, oval, angular or comma-shaped density most commonly at the base of the lung posteriorly, although it has been described elsewhere in the chest (Benard *et al.*, 1973; Brune *et al.*, 1974; Choffel *et al.*, 1977; Fadhli and Derrick, 1965; Hanke, 1971; 1972; Hanke and Kretzschmar, 1980; Heine, 1962; Kretzschmar, 1975; Roche *et al.*, 1956; Roche and Rousselin, 1957; Schneider *et al.*, 1980). It does not conform to segmental or lobular orientation. RA is generally preceded by a pleural effusion, but has been described following therapeutic pneumothoraces. Recognition of this type of pulmonary collapse and its differentiation from other pathological processes which may present as a pulmonary mass density are important to avoid unnecessary surgery. The purpose of this report is to describe our experience with RA and further to evaluate its pathogenesis and radiographic appearance.

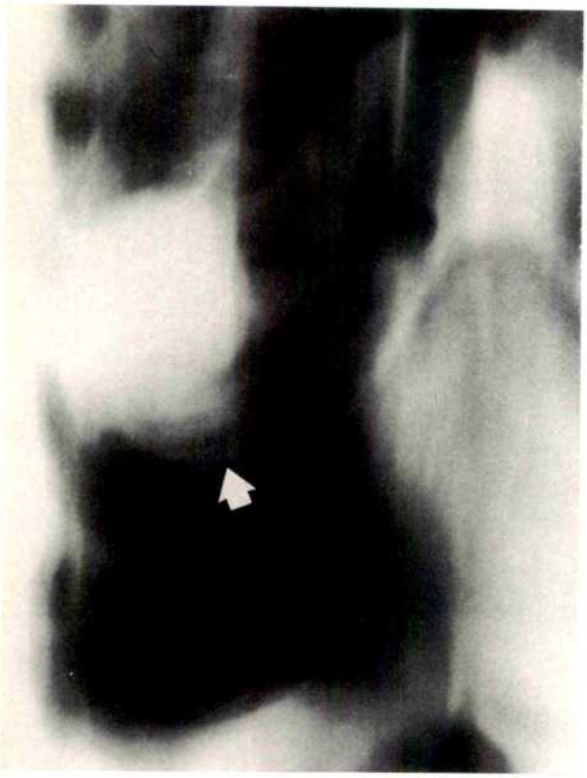


Fig. 1d.

A tomogram, lateral cut, through the middle portion of the mass demonstrates multiple pulmonary vessels encircling the mass in a helical fashion (arrow).

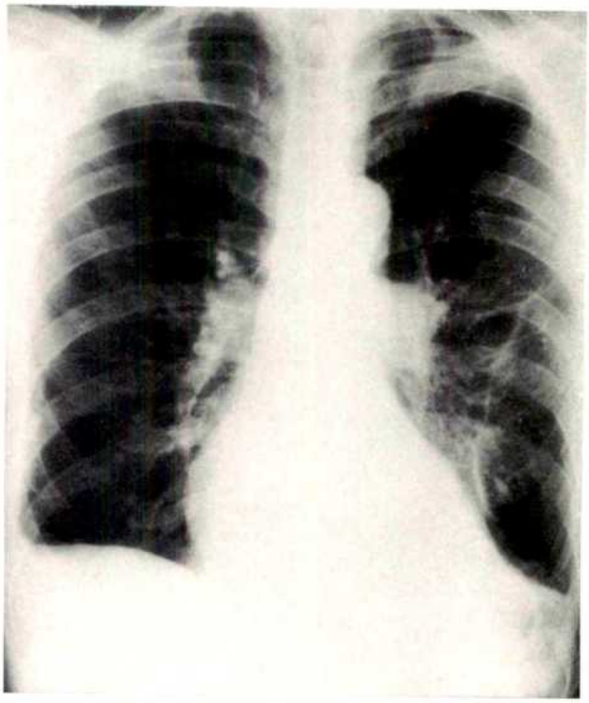


Fig. 1e.

Post-operative chest radiograph shows no residual mass in the lung.

CASE REPORTS

Case 1

A 62-year-old black man was admitted to a local hospital with a one-year history of intermittent gross haematuria. The urological evaluation revealed a Grade II transitional cell carcinoma of the bladder. The patient was transferred to our institution for further evaluation and therapy.

Past medical history was significant in that the patient had had spinal surgery for spur removal in 1971 and had a recent bout of pneumonia in 1977. He has smoked heavily for many years and admitted "bronchial trouble" and chronic shortness of breath on exertion.

Pertinent physical findings included moderately decreased breath sounds over the right lower chest posteriorly as well as a slight fullness in the left side of the lower abdomen above the pubic symphysis. The rest of the physical examination was unremarkable.

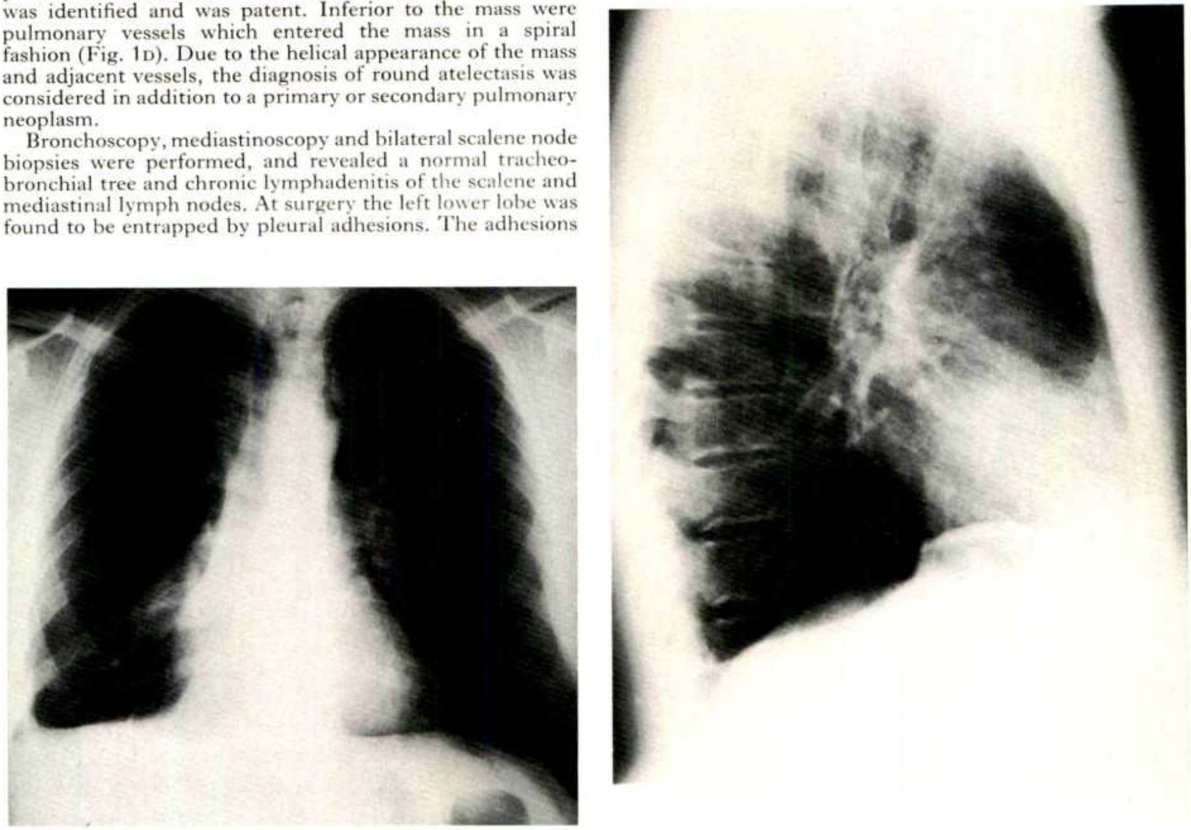
Laboratory data included a haemoglobin of 13.3 g% and a urinalysis which demonstrated numerous WBCs and 15 to 20 RBCs per high power field. The chest radiographs demonstrated a 4 cm mass density localized in the superior segment of the left lower lobe. Also noted was overexpansion of the left upper lobe with downward displacement of the left hilum (Fig. 1A, B). Comparison with a chest radiograph one month earlier demonstrated that the mass had grown slightly in the interval. Linear tomograms of this mass demonstrated it to be round and well demarcated without any significant internal features. Linear densities were noted to extend from the mass toward the posterior chest wall suggesting pleural involvement (Fig. 1C). The proximal portion of the left lower lobe superior segmental bronchus was identified and was patent. Inferior to the mass were pulmonary vessels which entered the mass in a spiral fashion (Fig. 1D). Due to the helical appearance of the mass and adjacent vessels, the diagnosis of round atelectasis was considered in addition to a primary or secondary pulmonary neoplasm.

Bronchoscopy, mediastinoscopy and bilateral scalene node biopsies were performed, and revealed a normal tracheobronchial tree and chronic lymphadenitis of the scalene and mediastinal lymph nodes. At surgery the left lower lobe was found to be entrapped by pleural adhesions. The adhesions were lysed and decortication was performed allowing the left lower lobe immediately to reinflate. Histological examination of portions of resected pleura revealed only inflammatory changes. Post-operative chest radiographs showed no residual mass (Fig. 1E). The surgical and pathological findings confirmed the radiographic impression of RA. The patient recovered uneventfully and was discharged one week after thoracotomy.

Case 2

A 52-year-old healthy white male presented to his personal physician for a routine physical examination. He had no specific complaints. During the course of this examination a chest radiograph revealed a pulmonary mass lesion and the patient was referred to our institution for further evaluation.

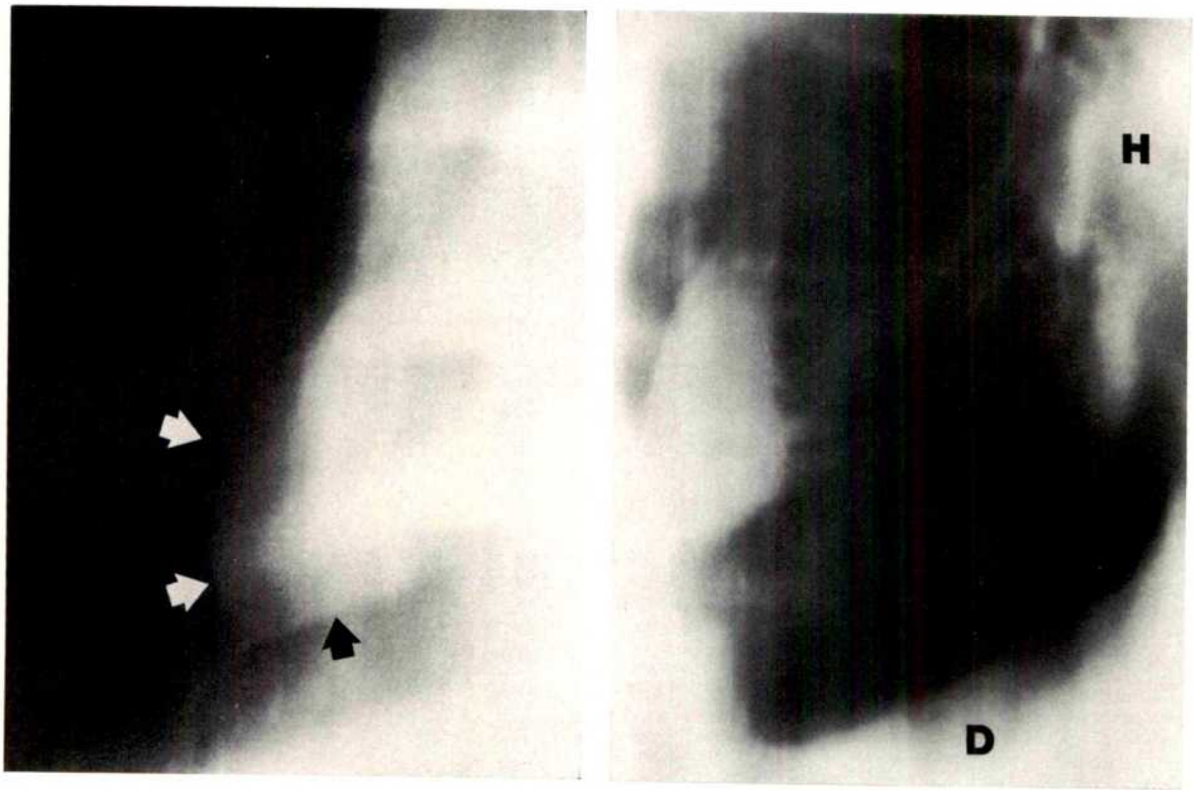
Historically, the patient has accumulated 70 pack years of smoking and also had a history of asbestos exposure several years previously. He denied cough, shortness of breath, haemoptysis, bronchitis or pneumonia. On physical examination the only pertinent findings were soft rhonchi on auscultation and a slightly prolonged inspiratory phase. Laboratory and ECG findings were unremarkable. A chest radiograph demonstrated diffuse pleural thickening on the right as well as obliteration of the right lateral and posterior costophrenic sulci. No definite pleural calcifications were detected. In addition there was a 4 × 6 cm mass noted posterior and medially in the right lower lobe. It projected behind the right heart border and was vaguely identified over the thoracic spine on the lateral view (Fig. 2A, B).



A FIG. 2. B

(A) PA and (B) lateral views of the chest reveal a 4 × 6 cm mass at the posterior portion of the right lower lobe, behind the right heart border. Diffuse pleural thickening is noted as well.

UNIVERSITY COLLEGE OF MEDICINE LIBRARY G. U.



C

Fig. 2.

D

Tomograms, (C) AP and (D) lateral cuts, demonstrate an oval shaped soft tissue mass attached to the pleural surface posteriorly. There are multiple pulmonary vessels encircling this mass in a coiled fashion. D = Diaphragm; H = Hilum.

Tomographic examination of this mass in both the AP and lateral projections demonstrated a soft tissue mass which was somewhat oval in shape and attached to the pleural surfaces posteriorly. There were multiple pulmonary vessels encircling this mass in a coiled fashion (Fig. 2C, D). Round atelectasis was the radiographic impression. However, due to the patient's smoking history and the previous exposure to asbestos, we felt compelled to exclude a bronchogenic carcinoma. Bronchoscopic examination was performed and was normal. Needle aspiration biopsy of the mass yielded no evidence of an inflammatory process. Two Cope needle biopsies at the same site followed and the histological diagnosis of chronic pleuritis and asbestosis was made. There was no evidence of malignancy. Due to the radiographic findings and the histological information obtained, it was determined that this patient should be discharged and followed in the chest clinic. His chest radiographs have remained unchanged for one year.

Case 3

A previously healthy 54-year-old white male suffered blunt trauma to the left side of his chest. The patient experienced pain but did not seek medical attention at this time. Three months after this episode on a routine physical examination, an abnormal density was identified in the left lower lung field on chest radiograph. He was subsequently referred to this institution for evaluation. He had been asymptomatic in the interval between the traumatic event and the physical examination. Past medical history was unremarkable except that the patient was a smoker. Physical examination on admission was unremarkable. The examination of the chest was normal. Chest radiographs at admission demonstrated a 3.5 × 4.5 cm oval mass localized to the superior segment of the left lower lobe. Pleural adhesions were identified at the left base, as was some hyperexpansion of the left upper lobe with downward displacement of the left hilum (Fig. 3B, C). Previous chest radiographs one-and-a-half years before admission demonstrated only basal pleural adhesion (Fig. 3A). AP tomographic examination demonstrated an oval mass density posteriorly with clearly defined air bronchograms within the mass (Fig. 3D). At thoracotomy, the pleura was markedly thickened and scattered areas of cholesterol and hyaline depositions were noted. There was a massive contraction of the left lower lobe particularly involving the superior, posterior basal and lateral basal segments. There was marked distortion of the lung secondary to the contraction giving rise to a mass-like appearance. Decortication was undertaken and the lower lobe was carefully unfolded, revealing no mass. Biopsies of the pleura demonstrated only hyaline deposition and fibrosis. There was no evidence of malignancy. Post-operative chest examinations demonstrated re-expansion of the left lower lobe. Follow-up chest examinations demonstrated no evidence of recurrent atelectasis (Fig. 3E).

DISCUSSION

Loeschke (1928) gave the first description of helical or rounded pulmonary atelectasis in his discussion of collapse associated with pleural effusion. He made the key observation that the lower edge of the lung became folded on itself due to pressure

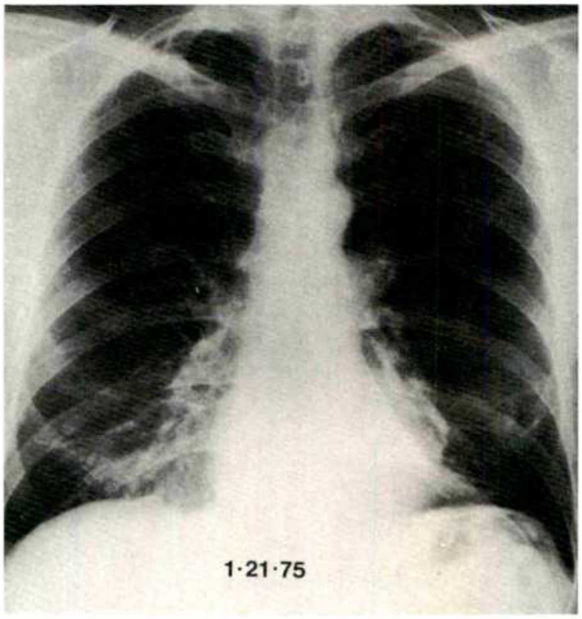
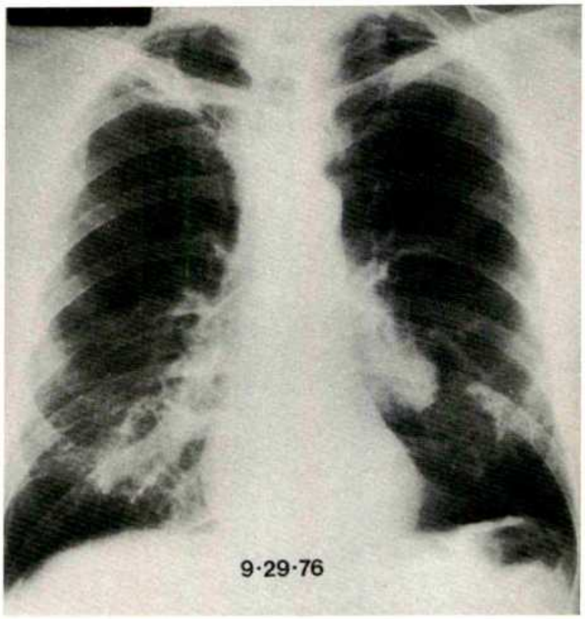


FIG. 3A.

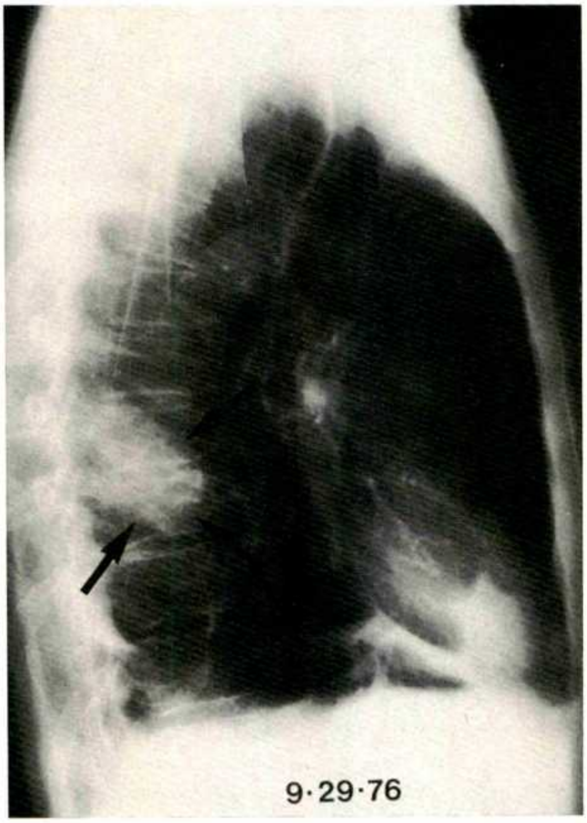
PA view of chest obtained about a year and a half prior to admission reveals non-specific chronic interstitial disease and pleural adhesions at both bases.



B

exerted by the pleural fluid. Schummelfeder (1956) confirmed this finding and concluded that the enfolding of the lung can occur not only in an upright and backward fashion, but also in a downward and diaphragmatic direction as well. Roche *et al.* (1956; 1957) described lung opacities in patients who had undergone therapeutic pneumothorax for tuberculosis. They attributed these opacities to atelectasis secondary to neurovascular reflexes, although they did consider the lung folding on itself. Heine (1962) described several cases of mass-like atelectasis in patients following therapeutic pneumothoraces, which he either resected or successfully re-inflated after decortication. However it is Hanke's report in 1971 that most clearly described this type of atelectasis (Fig. 4A–D).

In the common form of atelectasis, the radiographic presentation is that of a triangular area of increased density corresponding to the lobe or segment involved. This appearance depends on the



C

FIG. 3.

(B) PA and (C) lateral views of the chest on admission reveal a 3.5 × 4.5 cm oval mass at the superior segment of the left lower lobe (arrows). Pleural plaques at the left base are better seen in the lateral projection. Compensatory expansion of the left upper lobe with downward displacement of the left hilum is noted on the PA view.

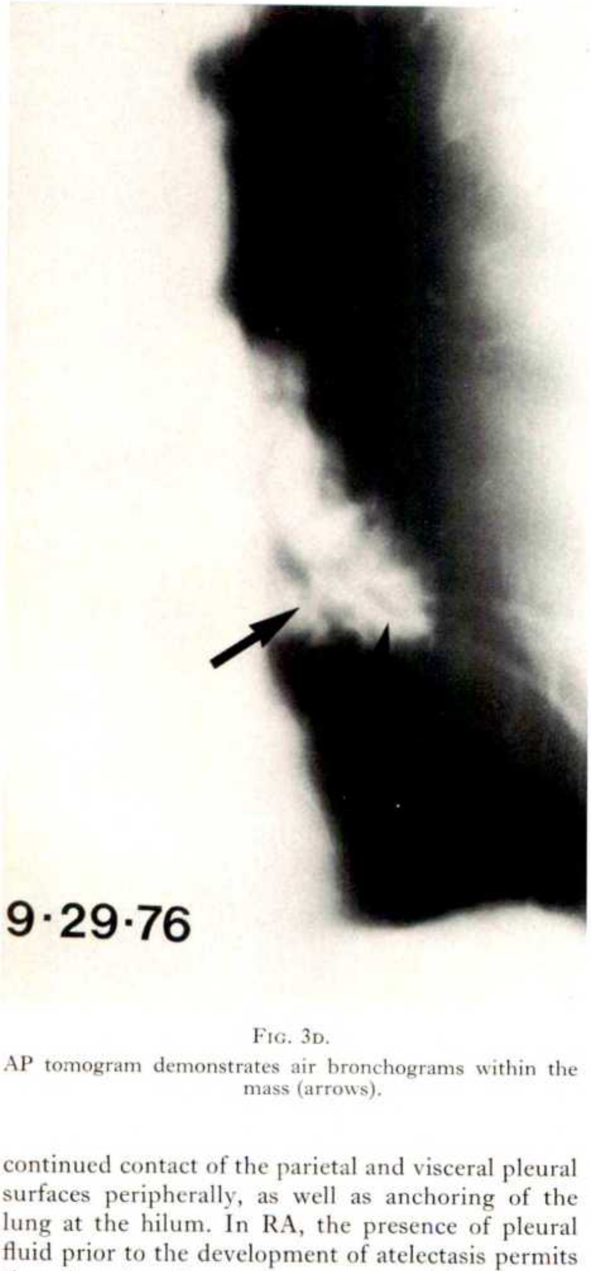


FIG. 3D.
AP tomogram demonstrates air bronchograms within the mass (arrows).

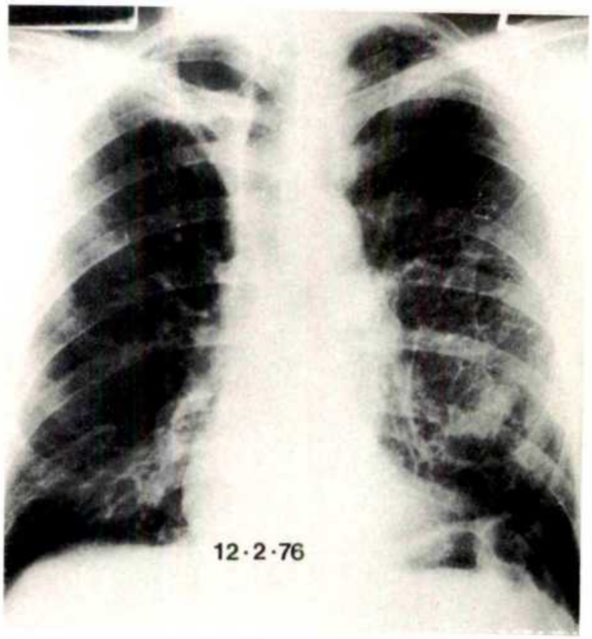


FIG. 3E.
PA view of the chest taken two months after surgery shows good expansion of the left lung with no evidence of recurrent atelectasis.

continued contact of the parietal and visceral pleural surfaces peripherally, as well as anchoring of the lung at the hilum. In RA, the presence of pleural fluid prior to the development of atelectasis permits the pleural surfaces to separate, and isolates the finger-like projection of lung, actually shaped like an inverted pyramid, in the posterior costophrenic sulcus (Fig. 4A). This isolation allows the pleural fluid to compress all of that portion of lung except for the base of the pyramid. Ultimately, transpulmonary pressure is increased under the effusion and eventually exceeds intraluminal airway pressure and collapse ensues. This process is favoured at the base of the lung due to the more positive pressure at the base of the pleural space relative to the apex, and gravity may play a role as well. A similar process occurs in pneumothorax. Once again the pleural surfaces are separated and portions of the lower lobe are flattened out in finger-like projections. This probably accounts for the appearance of this entity in patients following therapeutic pneumothoraces.

The enfolding process begins with either a clockwise or counter-clockwise rotation of the lower lobe bronchi (Fig. 4B, D). Rotatory movement is very likely aided by diaphragmatic activity during normal respiration. Once the rotation reaches the point at which the airway becomes kinked, atelectasis becomes more complete and the collapsed portion assumes a more flattened shape. As a result of the rotatory process, this flattened portion of lung comes to lie adjacent to the remaining portions of the lower lobe, either posteriorly or inferiorly. Their visceral pleural surfaces are juxtaposed and over a period of time a fibrinous bond forms between these surfaces and the nucleus of RA is formed (Fig. 4B).

As the effusion resolves and the pleural space is cleared, adhesions and areas of pleural thickening remain. Re-expansion of the lung, altered by the adhesions and pleural thickening, coils the nucleus of RA (Fig. 4C, D). Normal respiration causes the nucleus to become further enfolded and it assumes an oval, spherical, or angular shape. Its shape depends on the elastic recoil properties of the chest wall and the lung and to what degree they are influenced by pleural adhesions and scarring. With fewer adhesions, one might expect a more rounded appearance.

The evolution of RA takes several weeks or months. Once present, it may persist unchanged for a year or more, increase in size (Choffel *et al.*, 1977), regress or even totally disappear (Hanke, 1971). It has also been observed to re-appear following re-expansion via decortication (Schneider *et al.*, 1980).

Factors favouring the formation of round atelectasis include the presence of a pleural effusion, most commonly an exudative effusion. Inflammation of the pleural surfaces would favour the deposition of fibrin which would be important in producing the bond between the juxtaposed visceral surfaces in the enfolding process. It is noteworthy that this entity has frequently been described in the French and German literature in patients with tuberculosis, or with asbestosis as in our case and others (Schneider *et al.*, 1980; Blesovsky, 1966). The pleural effusions in these entities are quite similar and are both exudative.

The depth and AP dimension of the posterior costophrenic sulcus are important since the deeper and narrower the sulcus, the more likely it is that the lung residing in such an angle would be subject to compression in this process. Also the deeper the angle, the more likely it is that the projection of the lung would be influenced by diaphragmatic activity and displaced by the diaphragm once the rotatory movement has begun.

The radiographic findings in this process include a mass density which may assume a round, oval, angular or comma-like shape. The mass is pleural based. Air bronchograms may be seen within the mass (Fig. 3D). The bronchovascular bundles adjacent to the mass assume a helical arrangement as if they were being pulled into this mass density. This is best demonstrated via lateral tomography. Radiating linear densities originating in the area of the mass are sometimes seen and are thought to represent tethering of the pleura resulting from the enfolding process (Fig. 1C). Elsewhere in the hemithorax, there is evidence of pleural disease such as pleural thickening, blunting of the costophrenic angles, a shrunken hemithorax, or pleural calcification. Without obvious evidence of pleural disease, the diagnosis of RA should be suspect. Other signs of collapse may be present such as hyperaeration in the same lobe or in other lobes. Depression of the hilum on the ipsilateral side and altered position of the fissures may also be seen. This diagnosis must be considered in any pleural-based mass lesion of lung, especially when associated with pleural disease and a

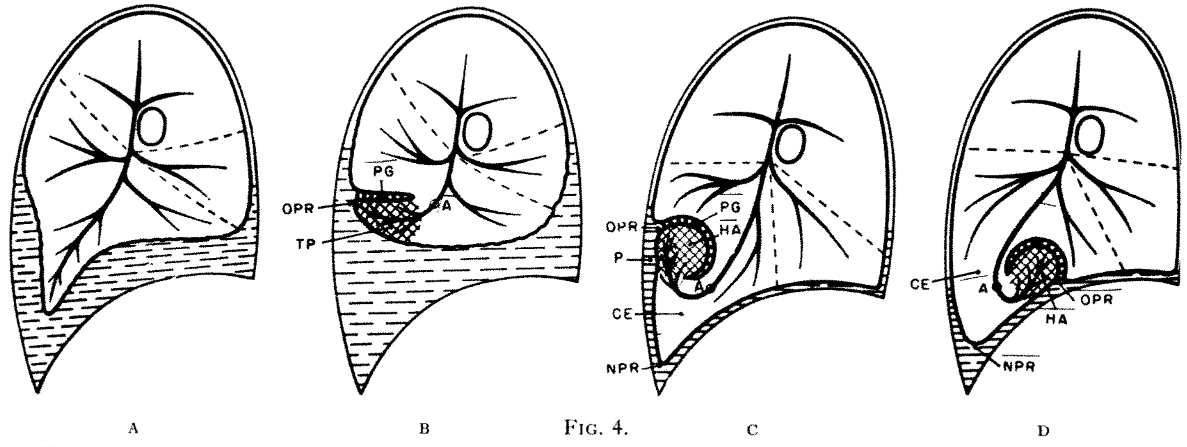


FIG. 4.

(A) The compression effect of the pleural effusion on the lung and the finger-like projection of the lung edge due to partial atelectasis is seen in the posterior costophrenic angle (From Hanke (1971), with permission).

(B) The tilted lung edge is pushed against the base of the lung and a pleural groove is formed following this folding process. When fibrin deposits cause these apposed pleural surfaces to stick together, it forms the nucleus of the round atelectasis (From Hanke (1971), with permission).

(C) After the resolution of the pleural effusion, the re-expanding force from the adjacent normal tissue causes atelectatic portion of the lung to assume a more rounded appearance. This coiling causes the helical appearance of the adjacent bronchovascular bundles (From Hanke (1971), with permission).

(D) The same process developing in the pulmonary base above the diaphragm is illustrated (From Hanke (1971), with permission). A = axis of rotation; CE = compensatory emphysema; HA = round (helical) atelectasis; NPR = new visceral pleural reflection at costophrenic angle; OPR = original visceral pleural reflection at costophrenic angle; P = pachypleurisy; PG = pleural groove; TP = tilted pleural surface.

previous effusion or pneumothorax, but requires recognition of a mass density associated with a helical arrangement of adjacent bronchovascular structures in the chest (Figs. 1d, 2d). When this constellation of radiographic findings is present, round atelectasis should be considered.

ACKNOWLEDGMENTS

The authors would like to express their thanks for the language assistance given by Albert Ammann, M.D., Mrs. Mary B. Ammann and Karsten Konerding, M.D., for the German literature, and Robert Sims, Ph.D. for the French literature, and the excellent secretarial help from Mrs. Sharron Shackleford.

REFERENCES

Benard, J., Mandard, J. C., Evrard, C. and Lemenager, J., 1973. Opacité ronde pseudotumorale par atélectasie (à propos d'une observation). *Revue Française des Maladies Respiratoires, 11,* 1171–1177.

Blesovsky, A., 1966. The folded lung. *British Journal of Diseases of the Chest, 60,* 19–22.

Brune, J., Bosly, A., Bory, R., Perinetti, M., Wiesendanger, T. and Galy, P., 1974. Condensations parenchymateuses pulmonaires arrondies postpleurétiques: méchanisme physiopathologique. *Lyon Médical, 231,* 605–609.

Choffel, C., Verdoux, P. and Milleron, B., 1977. Les atélectasies rondes pseudotumorales sans antécédents pleuraux avères. *Le Poumon et le Coeur, 5,* 295–302.

Fadhli, H. and Derrick, J. R., 1965. Twisted lingula—a case of a solitary pulmonary nodule. *Annals of Thoracic Surgery, 6,* 753–754.

Hanke, R., 1971. Rundatelektasen (Kugel- und Walzenatelektasen): ein Beitrag zur Differentialdiagnose intrapulmonaler Rundherde. *Fortschritte auf dem Gebiete der Röntgenstrahlen, 114,* 164–183.

1972. Rundatelektasen: ihre differentialdiagnostischen Merkmale gegenüber intrapulmonalen Rundherden anderer Genese. *Kongressbericht Wissenschaftlichen Tagungen Norddeutsch-Gesellschaft für Tuberkulose und Lungenkrankheit, 12,* 174–184.

Hanke, R. and Kretzschmar, R., 1980. Rounded atelectasis. *Seminars in Roentgenology, 15,* 174–182.

Heine, F., 1962. Faltungsphänomene der Lunge. *Internist, 3,* 357–363.

Kretzschmar, R., 1975. Über atelektatische Pseudotumoren der Lunge. *Fortschritte auf dem Gebiete der Röntgenstrahlen, 122,* 19–29.

Loeschke, H., 1928. *Henke-Lubarsch Handbuch der speziellen pathologischen Anatomie und Histologie.* 3. Bd., 1. Teil, (Springer, Berlin), p. 599.

Roche, G., Parent, J. and Daumet, P., 1956. Atélectasies parcelliares du lobe inferieur et du lobe moyen au cours du pneumothorax thérapeutiques. *Société Française de la Tuberculose* (Paris), *20,* 87–93.

Roche, G. and Rousselin, L., 1957. Opacités pulmonaires multiples dues au therapeutique. *Société Française de la Tuberculose* (Paris), *21,* 506–512.

Schneider, H. J., Felson, B. and Gonzalez, L. L., 1980. Rounded atelectasis. *American Journal of Roentgenoiogy, 134,* 225–232.

Schummelfeder, N., 1956. Umfaltungen und Verwachsungen an freien Lungenrandern. *Beiträge zur Pathologischen Anatomie, 116,* 422–435.

Book review

Radiology of Bone Disease. By George B. Greenfield, 3rd edit., pp. 858, 1980 (J. B. Lippincott, Philadelphia), £39·00. ISBN 0-397-50432-2

It is a pleasure to have the opportunity to review an enlarged third edition of a frequently used book in our departmental library. The author remains faithful to his stated aims, being to group diseases by predominantly radiographic features, to collate recent information and to advocate a systematic approach to diagnoses. There are accordingly nine sections reflecting this approach including an analytical approach to bone radiology, loss of bone density, alteration in bone texture, changes in size and shape of bone, etc. The volume is liberally sprinkled with illustrations, including plain films, isotopes, CT and angiography, and contains many full gamuts. There is a good index. A bibliography is given with each section comprising between 100 and 150 pertinent references.

Whether or not this book is well received will depend, to an unusual degree, on the reader's preferences. For example, the approach used results in diseases being scattered throughout the book in different sections. The authors' desire to incorporate clinical, laboratory and other features of various diseases seems sometimes excessive, with,for example, two pages on the clinical criteria for diagnosing rheumatoid arthritis, with perhaps some disadvantage to the description of the radiological signs of disease. Although liberally supplied with illustrations, a fair proportion are of relatively poor quality on reproduction. There is virtually no information on arthrography, myelography or venography and disappointingly few isotopic investigations. The really common problems such as trauma and the low back pain syndromes are hardly mentioned. The author's view, that it is no longer sufficient for radiology just to predict histology of bone lesions, is reflected in the frequent use of pathology to explain radiographic signs.

This book should be in the libraries of all training departments in radiology and will be frequently used as a bench book by those practising bone and joint radiology. It is not a substitute for basic texts to the training radiologist but rather complements the other authoritative tomes which every good department should have. Its concept is brilliant but it may be argued that it does not quite achieve its objective in practice.

Iain Watt.

1981, *British Journal of Radiology*, *54*, 651–654 AUGUST 1981

Benign greater curve gastric ulcer: the "sump-ulcer"

By *R. E. Kottler, M.B., Ch.B., M.Med.(Rad.D.) and R. J. Tuft, M.B., B.S., F.R.C.S.

Department of Radiology, Groote Schuur Hospital and University of Cape Town, Observatory, Cape Town 7925, South Africa

(*Received December 1980*)

ABSTRACT

Twenty-six cases of greater curve gastric ulcers are presented, of which all but one were benign. There appears to have been an increased occurrence of benign greater curve gastric ulcers in our institution. By using a double contrast barium examination diagnostic accuracy was high, although endoscopy and biopsy are required for confirmation. Greater curve gastric ulcers were commonest in elderly patients with concomitant disease and a high intake of oral drugs, particularly analgesics, potassium chloride supplements and steroids. The constant location of the ulceration in the most dependent part of the stomach suggests a causal relationship with drug ingestion in these patients. The term "sump-ulcer" is suggested. A relatively high incidence of perforation and gastrocolic fistulae was found. It would appear that gastrocolic fistulae from benign peptic ulcer disease, previously thought to be excessively rare, are becoming more commonly recognized.

The finding of an ulcer on the greater curve of the stomach often raises the spectre of malignancy, but it is now well established that most greater curve gastric ulcers (GCGUs) are benign (Findley, 1961; Lumsden, 1973). Our experience confirms this but suggests, furthermore, that the benign GCGU is a disease of elderly patients, many with concomitant disease who are taking multiple oral medication and analgesics.

Greater curve gastric ulcers are uncommon but it would appear that there has been a recent increase in incidence among our patients. These ulcers are prone to occasional perforation with formation of a gastrocolic fistula. This complication following benign peptic ulceration was once thought to be very rare, but is being more frequently encountered (Hitchens, 1972; Laufer *et al.*, 1976; Rabin and Philips, 1977; Karakousis and Greenberg, 1979).

Although benign and malignant ulcers may be found anywhere along the greater curve, all our ulcers were situated in the distal third of the stomach, with none in the proximal two-thirds. The concept of a "sump-ulcer" is therefore introduced, *i.e.* an ulcer situated in that part of the stomach which is the lowest when the patient stands up.

PATIENTS, METHODS AND RESULTS

In our series of 26 greater curve ulcers, seven were collected by one author (R.E.K.) between 1968 and 1978 and the remaining 19 cases were encountered in the period January 1979 to August 1980. A double contrast barium meal was used in most of the latter cases. Of the 19 recent cases, nine were in males and ten in females. The age range was 40–78 years (mean 62). The diagnosis was confirmed in all cases by endoscopy, endoscopic biopsy or from surgical specimens. With one exception, all the ulcers in this series were found to be benign. In the one case an ulcer was demonstrated within a large infiltrating carcinoma.

Ulcers were defined as being on the greater curve if they either projected from or overlapped the inferior margin of the stomach. The greater curve location was confirmed endoscopically. Cases in whom the endoscopist's siting of the ulcer did not correspond were excluded from our series. All the GCGUs were constantly located in the distal third of the stomach, in the most dependent portion when in the erect position (Fig. 1).

Three large ulcers had a diameter greater than 3 cm, 14 ranged from 0.5–2.5 cm and two were healed endoscopically. The latter showed striking

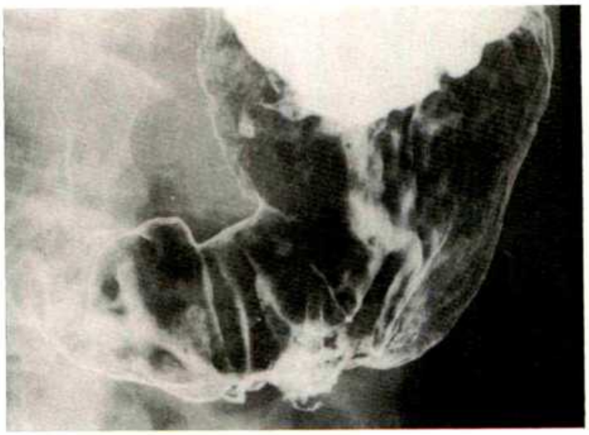


FIG. 1.

A 2 cm benign ulcer in the most dependent portion of the stomach, *i.e.* a "sump-ulcer". A 72-year old female suffering from CCF, taking diuretics, potassium supplements and analgesics for arthritis, being investigated for iron deficiency anaemia.

---

*Address for reprints: Prof. R. E. Kottler, Department of Diagnostic Radiology, Groote Schuur Hospital, Observatory, Cape Town 7925, South Africa.

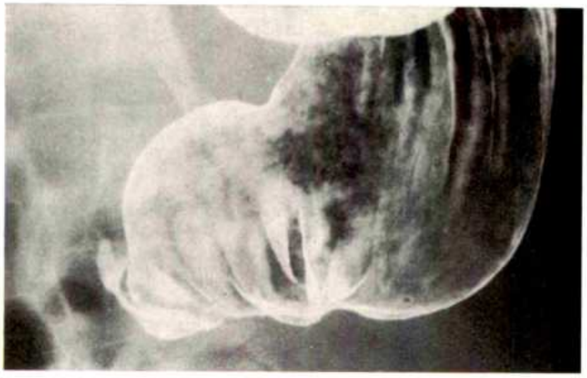


FIG. 2.

A healed greater curve gastric ulcer following a 1.5 cm ulcer demonstrated six weeks prior to this study. Note the striking fold radiation of the healed ulcer.

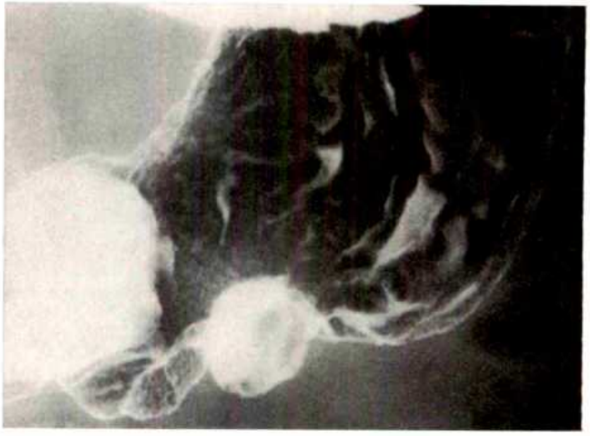


FIG. 3.

A typical 2.5 cm benign penetrating ulcer in the sump of the stomach showing a slightly "recessed" and "intraluminal" position simulating malignancy. All the ulcers in this series were located in this particular region of the stomach.

fold convergence on the double contrast barium meal and at endoscopy (Fig. 2).

The major complication encountered was perforation (6/26). Two of these perforations were acute, into the peritoneal cavity, and the remaining four produced gastrocolic fistulae. Of the four cases of gastrocolic fistulae two were suspected on barium meal examination, but barium enema remained the definitive procedure for diagnosis.

Of our recent 19 cases, records showed that 14 were receiving oral medication. Eight received diuretics and potassium supplements, and 11 took regular or occasional analgesics, but among these there were also two diabetics on oral therapy and two receiving steroids. The multiplicity of the diseases and treatment in these cases is striking but renders analysis difficult.

DISCUSSION

The previously reported incidence of GCGUs has been between 2.5 and 5.0% of all gastric ulcers, and the majority of them are benign (Findley, 1961). In most of our cases, especially where a good double contrast barium study was obtained, the probability of a benign ulcer could be predicted with reasonable confidence, but all were nevertheless referred for endoscopy and endoscopic biopsy to exclude malignancy.

There appears to have been an increased incidence of benign GCGUs in our institution. This may be due to a real increase but is also partly due to improved detection and to our greater awareness.

The profile radiological features of benign GCGUs have been described (Zboralske *et al.*, 1978). Our experience confirms those observations that in profile GCGUs may have an apparent intraluminal location, show a recessed appearance and have "shouldered" edges. The features which suggest malignancy on the lesser curve are therefore occasionally seen with benign ulcers on the greater curve (Fig. 3).

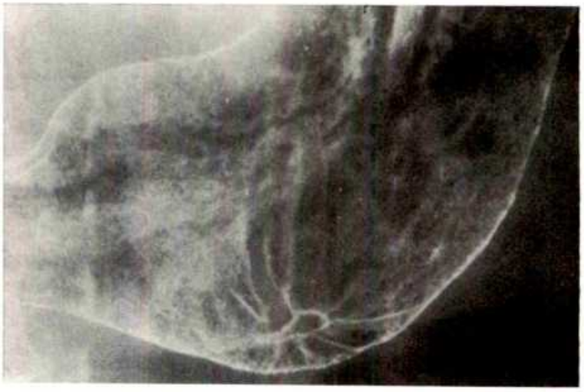


FIG. 4.

A 0.5 cm healing ulcer presenting in the shape of a ring with converging folds in a double contrast barium meal. A 64-year-old female taking oral anti-diabetic drugs, diuretics, potassium supplements and iron.

In three of our cases, the ulcer presented only radiological signs of converging folds, and evidence of a healed or healing gastric ulcer was found endoscopically. Such findings are recognizable only in double contrast barium studies (Fig. 4). On the other hand, the small bowel may obscure the greater curve in the double contrast examination, and in one case a

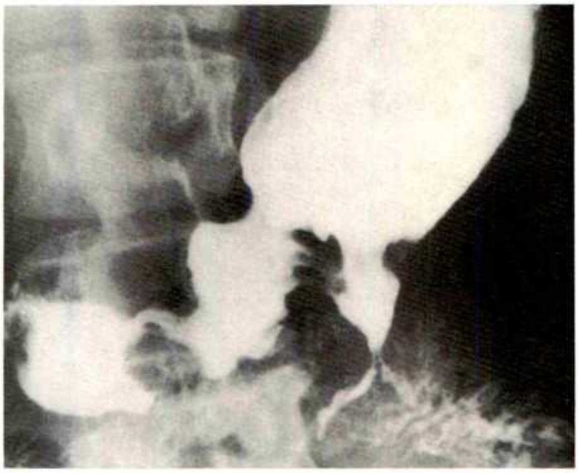


FIG. 5.

A 50-year-old female on oral analgesics complaining of dyspepsia and flatulence. Barium meal showed a "sump-ulcer" with a gastrocolic fistula.

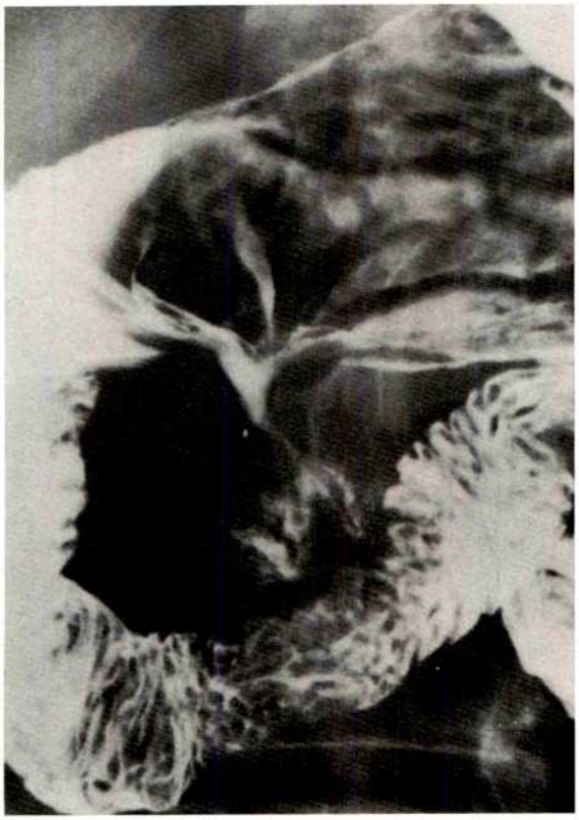


FIG. 6.

Barium meal showing ulcer with suspected gastrocolic fistula. This was confirmed by barium enema. A 67-year-old diabetic male taking drugs for arthritis.

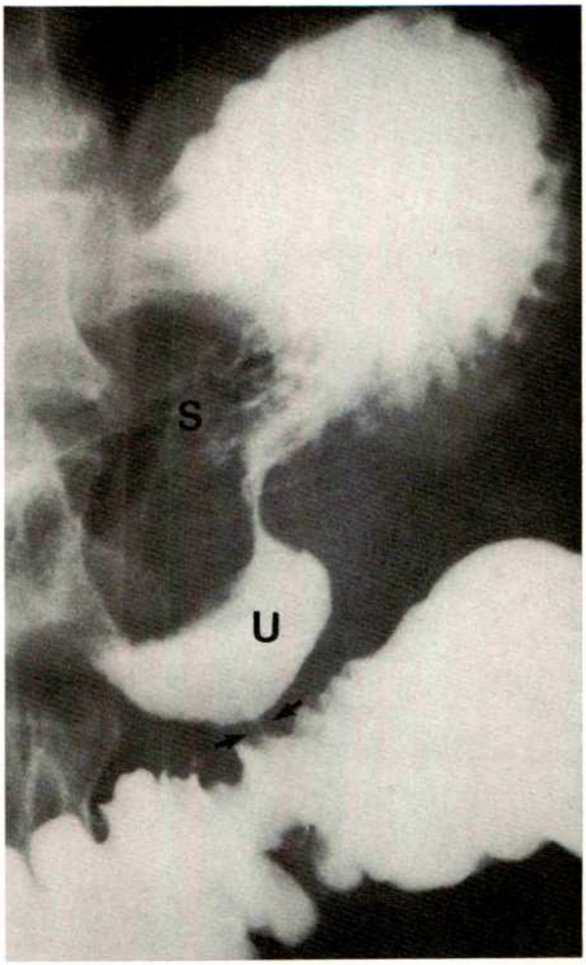


FIG. 7.

Barium enema showing gastrocolic fistula (arrows) arising from a large gastric ulcer (U) on the greater curve of the stomach (S) in a 52-year-old male.

7 cm GCGU could only be detected in subsequent single contrast compression views.

Ulcers have been described as occurring anywhere on the greater curvature of the stomach, but in our experience greater curve ulcers in the proximal two-thirds of the stomach are exceptionally rare, and we have not encountered any during the period of this study. The correlation between the radiological greater curve and endoscopic greater curve was not always straightforward; hence we have confined ourselves to ulcers in which there was endoscopic agreement.

Our cases showed an equal sex ratio, but GCGU does appear to be a lesion of elderly patients (mean age 62 years). It became apparent that the patients had a high incidence of concomitant disease (cardiac failure, diabetes, "arthritis") and the majority were on multiple medications for this. The multiplicity of the medication made it difficult to incriminate any particular drugs with certainty, but potassium chloride, analgesics and steroids are gastric irritants. The constant location of the ulcer in the most dependent portion of the stomach in the erect position is noteworthy and it is tempting to postulate that tablets may collect in this particular area and produce irritation. The term "sump-ulcer" is suggested for GCGUs in this situation.

Complications were encountered in six of our 26 cases. There were two acute intraperitoneal perforations and four gastrocolic fistulae (Figs. 5, 6, 7). While the majority of gastrocolic fistulae is thought to be due to malignant disease, their association with benign peptic ulcer disease has become increasingly recognized. Martel (1977) reviewed the English literature and found that 47 cases had been recorded due to benign peptic ulcer. Rabin (personal communication, 1980) has had a total experience of eight gastrocolic fistulae, only one of which was malignant.

In conclusion, these experiences are reported to draw attention to the location, aetiology and complications of benign peptic ulcers of the greater curve.

REFERENCES

Findley, J. W., 1961. Ulcers of the greater curvature of the stomach. *Gastroenterology, 40,* 183–187.

Hitchens, E. M., 1972. Benign gastric ulcer as a cause of gastrocolic fistula. Report of a case and review of the literature. *Archives of Surgery, 104,* 108–109.

Karakousis, C. P. and Greenberg, P. H., 1979. Gastrocolic fistula as a complication of benign gastric ulcer. *Archives of Surgery, 114,* 1426–1428.

Laufer, I., Thornley, G. D. and Stolberg, H., 1976. Gastrocolic fistula as a complication of benign gastric ulcer. *Radiology, 119,* 7–11.

Lumsden, K., 1973. Gastric ulcers on the greater curve. *British Journal of Radiology, 46,* 154.

Martel, W., 1977 (Ass. Ed.) *Recent Advances in Diagnostic Radiology* (Year Book Medical Publishers Inc., Chicago), p. 261.

Rabin, M. S. and Philips, R. L., 1977. Benign gastric ulcer as a cause of gastrocolic fistula. *South African Medical Journal, 51,* 990.

Zboralske, F. F., Stargarter, F. L. and Harell, G. S., 1978. Profile roentgenographic features of benign greater curvature ulcers. *Radiology, 127,* 63–67.

Book review

Renal Microvascular Disease Angiographic-Microangiographic Correlates. By Joseph J. Bookstein and Richard L. Clark, pp. xx+451, illus. 1980 (Little, Brown & Co., Boston), $49.00.
ISBN 0-316-10237-7

There are 20 pages with Roman numerals to be got through at the start of this book, but do not be put off. Stuff like "aspects of beauty and excitement" and "state of the art" makes dutiful, tired bows here. Once the titles have stopped rolling, better, stunning things lie in wait. We have known for several years that these two authors were jointly at work, combining Bookstein's *in vivo* magnification angiograms with Clark's *in vitro* microangiography. The result is a remarkable volume. The language is uncluttered, the illustrations ravishing. The reader is led through basic angiogram concepts, normal anatomy and blood flow, to an angiographic classification of renal parenchymal disease. The classification is expanded in the following chapters: first acute and chronic loss of glomerular granularity, and then interlobar occlusive disease. Later chapters home in on pathological entities like pyelonephritis, renal infarction and ischaemia, hypo- and hypervascular masses. The emphasis is always on making sense of the clinical angiogram in the light of histology, pathophysiology and microangiography. The transplanted kidney is not forgotten.

The authors are not only clear but honest. "A one-to-one correlation between angiographic pattern and histologic classification of disease does not exist" (p. 57); "microinfarcts (these do not reproduce adequately on this illustration)" (p. 134); for ATN and acute rejection in the transplanted kidney "in general, angiographic differentiation is not reliable" (p. 364). You may have doubts about what is said in the book—if so, it is probably the authors who have stimulated you in this direction.

Bookstein and Clark stake out a field, plough it, and put down seeds. This is well done, and full of insights. Did you know that one may find renal vascular malformations (angiodysplasia) in patients without haematuria? Interestingly, a current British obsession, the recurrent loin pain-haematuria syndrome, receives no more than mention.

I think that anyone interested in the kidney will wish to study if not own this book.

Thomas Sherwood.

1981, *British Journal of Radiology*, *54*, 655–659 AUGUST 1981

Pre-operative computed tomography of carcinoma of the rectum

By *A. K. Dixon, M.A., M.R.C.P., F.R.C.R., I. Kelsey Fry, D.M., F.R.C.P., F.R.C.R.

Department of Radiology, St. Bartholomew's Hospital, London EC1

B. C. Morson, F.R.C.P., F.R.C.S., F.R.C.Path., R. J. Nicholls, M.Chir., F.R.C.S. and

A. York Mason, B.Sc., F.R.C.S.

Departments of Pathology, Surgery and Research, St. Mark's Hospital, London EC1

(*Received December 1980*)

ABSTRACT

Fifty-two patients with carcinoma of the rectum underwent computed tomography (CT) in the immediate pre-operative period. CT was used in order to assess extrarectal tumour spread. The resected specimen was staged by the pathologist who subdivided spread in continuity beyond the bowel wall into slight, moderate or extensive. In 21 out of 23 patients with no or slight extrarectal local spread CT showed normal perirectal fat. Extrarectal spread was demonstrated by CT in eight of the nine patients found to have extensive local spread. This was seen to be circumferential in the only two patients with inoperable tumours. CT identified discrete nodal enlargement in seven of the 18 patients with histologically involved lymph nodes. CT may help the less experienced surgeon, especially when he is not confident of his findings at digital examination. CT allows assessment of high rectal tumours which cannot be examined digitally. It may play a role where a tumour with extensive local spread is clinically suspected and confirmation is needed before pre-operative radiotherapy is given.

Reliable pre-operative determination of the extent of spread of a rectal carcinoma would not only indicate the expected prognosis but might also assist management. Those patients in whom the local spread was known to be extensive might benefit from pre-operative radiotherapy. The surgeon would be forewarned of patients in whom resection may prove difficult.

The diagnosis of rectal carcinoma largely rests on digital and proctoscopic examination. The barium enema, while outlining the intraluminal component of the rectal lesion, does not provide much information about the degree of extrarectal spread.

Digital examination can reveal the size and fixity of the tumour and the presence of extrarectal growth. However it may be difficult to obtain a reliable digital assessment, especially with high rectal tumours and in obese patients. Furthermore, the accuracy of the examination may depend upon observer experience.

Computed tomography readily demonstrates perirectal fat (Fig. 1A, B) and extrarectal tumour spread into this fat should show up well. Accordingly it seemed possible that computed tomography might have a role in staging rectal cancer. We have com-

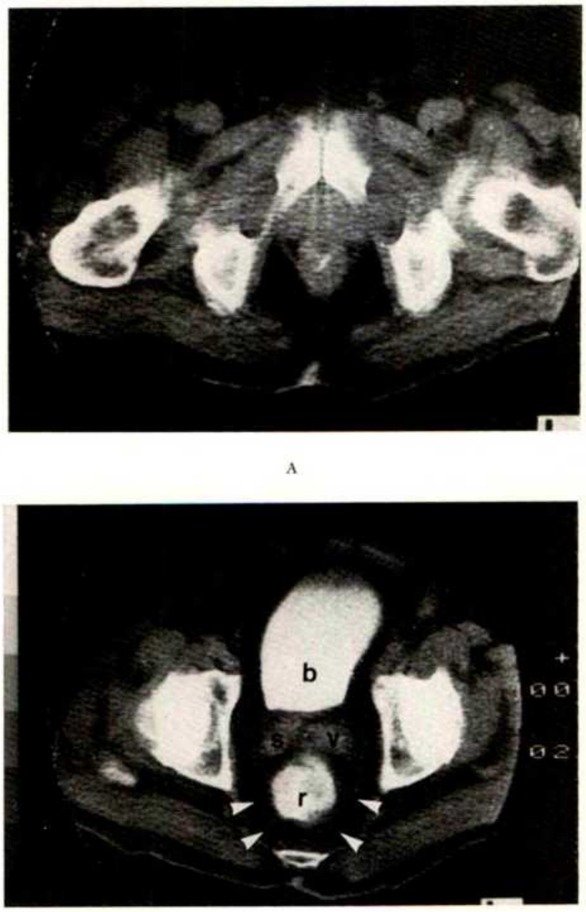


FIG. 1.

Two CT scans through a normal male pelvis. Dilute contrast medium instilled per rectum. This patient had also received intravenous contrast medium and thus the bladder appears opaque.

(A) Normal ischiorectal fossae containing fat. A trace of contrast medium can be seen in the most caudal part of the rectum.

(B) 3.9 cm cephalad to Fig. 1A. Seminal vesicles (s.v.) between bladder (b) and rectum (r). Non-homogeneity of rectum compatible with faeces mixing with the contrast medium. Normal perirectal fat surrounded by normal perirectal fibrous tissue (arrows).

---

*Present address and address for reprints: University Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

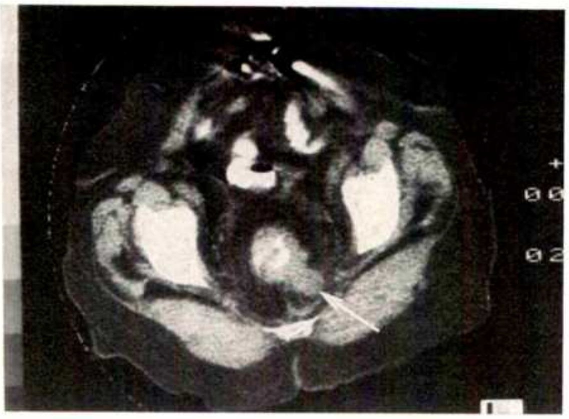


FIG. 2.

CT scan showing tumour (arrowed) extending into the perirectal fat from the main tumour on the left posterolateral wall of rectum. Subsequent histology proved that the local spread was extensive.

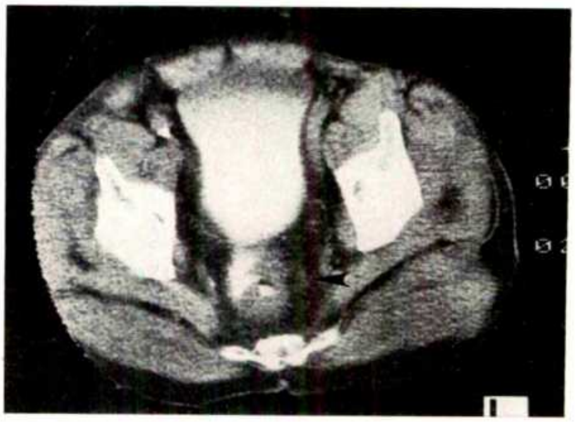


FIG. 3.

CT scan showing a discrete soft tissue shadow within the perirectal fat (arrowhead), separate from the soft tissue density rectal tumour at this level. This was correctly interpreted as nodal enlargement. The tumour is seen as an irregular filling defect on the left of the rectum—the contrast medium is displaced anteriorly and to the right—the tumour was not thought to extend beyond the expected confines of the rectum. At microscopy there was in fact moderate local spread, together with involved pararectal nodes.

pared the extrarectal spread shown by CT with the degree of spread found by the pathologist in the excised specimen.

PATIENTS AND METHODS

Fifty-two consecutive patients with carcinoma of the rectum who were admitted for surgery to St. Mark's Hospital underwent computed tomography of the rectum in the immediate pre-operative period.

Fifteen millilitres sodium meglumine diatrizoate solution (Gastrografin) diluted to 300 ml with water were given orally 40 minutes before, and again immediately before scanning, so that small bowel loops would be opacified, and 100 ml of similarly diluted Gastrografin was instilled per rectum in order to delineate the rectosigmoid colon. Hyoscine-*n*-butyl bromide (20 mg IV) was used to control peristaltic artefact. The patient had previously been instructed not to void. As the study progressed it became apparent that interpretation was more straightforward when the bladder was full. Accordingly intravenous frusemide (20 mg) was occasionally given. Early in the study we employed a localizing device of graduated radiopaque catheters taped to the patient's skin. Because this technique caused considerable artefact shadowing it was subsequently abandoned. An EMI 5005 (18 seconds) scanner was used. This scanner produces a scan thickness of 1.3 cm. Contiguous slices were obtained from the pubic symphysis upwards until sigmoid colon was encountered.

The presence or absence of abnormal soft tissue shadowing within the perirectal fat was recorded. If continuous with the tumour, this was recorded as evidence of direct extrarectal spread (Fig. 2); if separate from it nodal enlargement was reported (Fig. 3). The level of the tumour (in cm from the anal verge) was known at the time of scanning. At the start of the study we sometimes found interpretation difficult because of our limited knowledge of cross-sectional pelvic anatomy, difficulty in estimating the precise position of the bowel wall and partial volume problems where the rectum was tortuous. However, at the end of the series when we had obtained more experience of pelvic scanning, one of us (I.K.F.) reviewed all the scans without knowedge of the operative findings. These review interpretations form the basis of this report.

Surgery was always carried out within two weeks of the CT examination and the resected specimen was staged by the pathologist. Extrarectal spread in continuity with the tumour was subjectively subdivided into slight (<1 cm), moderate (1–2 cm) or extensive (>2 cm). The lymph nodes were charted with respect to site and size and subsequently examined for involvement.

RESULTS

In five patients CT was unsatisfactory due to metallic artefact shadowing: three had metallic hip replacements and two had copious barium retention from a previous barium enema. The CT findings in the remaining 47 patients are compared with the pathological findings in Table I. As it was considered that CT would be unable to detect slight (<1 cm)

TABLE I

CT ASSESSMENT OF DIRECT EXTRARECTAL SPREAD

Pathological findings	No. of patients	CT	
		No spread	Spread
No spread or slight spread	23	21	2
Moderate spread	15	7	8
Extensive spread	9	1	8

TABLE II

CT ASSESSMENT OF NODAL INVOLVEMENT

Pathological findings	No. of patients	CT	
		No enlarged nodes	Enlarged nodes
No involved nodes	25	24 specificity = 96%	1
Involved nodes	18	11	7 sensitivity = 39%

extrarectal spread, we have grouped such tumours together with those with no extrarectal spread (their management will usually be similar). No spread was seen on CT in 21 of the 23 patients in this group. Spread was identified at CT in eight of the 15 patients with moderate spread, and in eight of the nine patients with extensive spread.

In four patients lymphatic involvement could not be assessed either because the tumour was inoperable or because local excision was performed. Comparison between the CT and pathological findings in the remaining 43 patients is shown in Table II. CT identified seven of the 18 patients with involved nodes (sensitivity 39%).

DISCUSSION

The results show that CT can be expected to demonstrate spread when this is more than 2 cm in extent, but appears unreliable in demonstrating lesser degrees of spread. Moderate local spread (1–2 cm) appears to be on the threshold of CT detection with spread seen in about half of such patients. This is very much what we would expect from experience gained in other areas of abdominal CT.

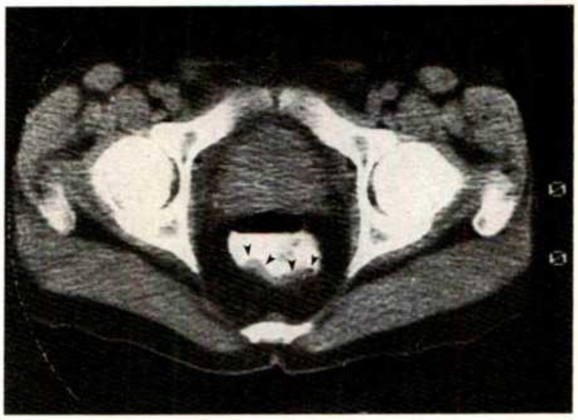


FIG. 4.

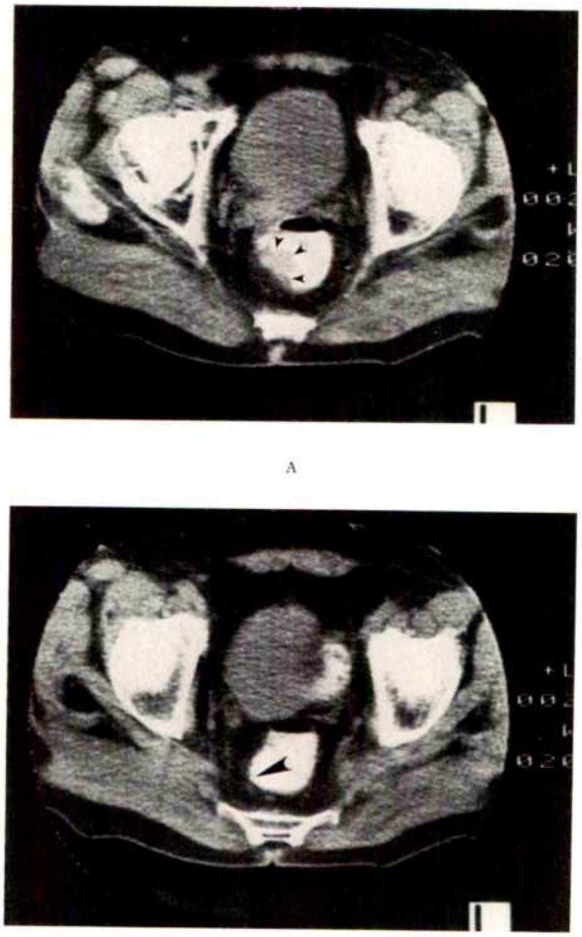
CT scan showing a posteriorly placed plaque-like tumour (small arrowheads). There is a prominent postrectal space (5 cm). On narrower window settings, the perirectal fat posteriorly appeared somewhat denser than elsewhere. This was interpreted as local spread but in truth there was no soft tissue density pararectal mass in continuity with the plaque-like tumour. Microscopy revealed slight (<1 cm) local spread.

The two patients with slight local spread in whom spread was thought to be present at CT illustrate problems of interpretation. In one there was a prominent postrectal space (5 cm) and the fat in this region appeared somewhat denser than elsewhere (this was considered to represent infiltration) (Fig. 4). In retrospect there was no true soft tissue mass in continuity with the tumour. In the other patient CT showed a very indistinct tumour margin peripherally with some apparent soft tissue shadowing lateral to this (Fig. 5A). Careful viewing of the cranially adjacent cut (Fig. 5B) showed that the rectum at this level was tortuous and that the apparent extrarectal spread was due to an indistinct rectal margin caused by partial volume effect. This latter problem was encountered frequently in the upper rectum which can be very tortuous.

CT failed to identify one patient with extensive local spread (Fig. 6). This patient was extremely thin with very little pararectal fat. Further confusion was caused by artefacts from the radiopaque localizing device. In retrospect the posterior margin of the rectum is poorly defined and, despite little pararectal fat, the presacral space is very indistinct.

In two of the patients there was such extensive local spread that the tumour was inoperable. In both these patients there was an identical CT appearance of a ring of soft tissue density around, and a slight distance away from, the rectum (Figs. 7, 8). This sign was not seen in any other patient in this series, but has been seen in one other patient with an inoperable tumour. It has also been seen in patients undergoing radiotherapy and has been described as the "halo" sign (Doubleday and Bernardino, 1980). The ring of soft tissue density is considered to represent perirectal fibrous tissue which may become thickened by tumour infiltration. If this sign indicates inoperability it might help management.

It is not surprising that only seven out of the 18 patients with involved nodes were identified, as CT will be most accurate in diseases where involvement causes enlargement and will be least accurate when nodes tend to be replaced with tumour but not necessarily enlarged (as in carcinoma of the rectum). Furthermore, in the pelvis the course of the lymphatic chains is oblique to the plane of the scans and normal vessels may be mistaken for enlarged nodes. Accordingly CT appears less accurate in assessing lymphadenopathy in the pelvis than in the para-aortic region (Korobkin *et al.*, 1979).


A

B

FIG. 5.

(A) CT scan through a tumour on the right posterolateral aspect of rectum (arrowheads). The perirectal fat alongside the tumour appears of higher density than elsewhere. This was interpreted as spread but microscopy revealed only slight (< 1 cm) local spread.

(B) Scan 1.3 cm cephalad to Fig. 5A shows the tortuosity of the rectum. A small portion of the eccentric expansion of the rectum (arrowhead) had probably been included on the cut shown in Fig. 5A (partial volume effect) and caused the misleading appearance.

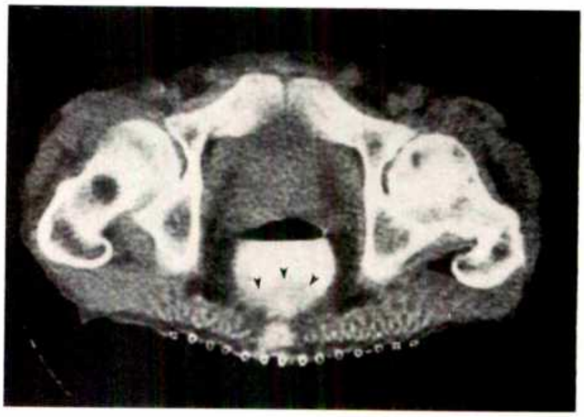


FIG. 6.

CT scan in a thin patient; the posteriorly placed tumour (small arrowheads) is seen within the intraluminal contrast medium. This was reported as showing no local spread. At surgery there was considerable extrarectal spread which proved extensive at microscopy. In retrospect the posterior margin of the rectum is poorly defined and, despite little perirectal fat, the presacral space is very indistinct. Further difficulty has arisen from the use of the localizing system of radiopaque catheters taped to the patient's skin. Artefacts from this device have partially obscured the region of interest in this thin patient.

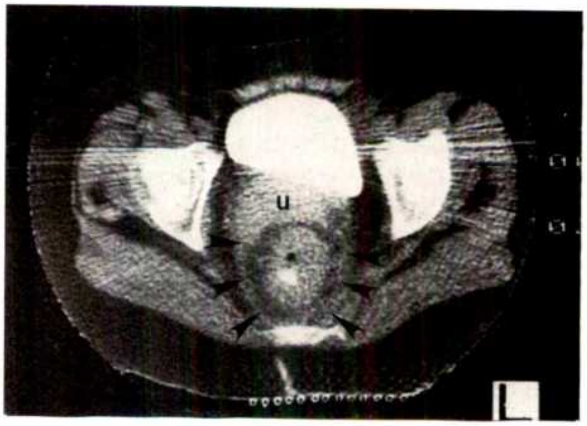


FIG. 7.

CT scan of a female patient with an inoperable carcinoma of the rectum. Note the ring of soft tissue density material (arrowheads) around, and at a slight distance away from, the rectum. The ring merges with the uterus (u) anteriorly. This was correctly interpreted as local spread. Indeed this sign of circumferential thickening of the perirectal fibrous tissue appears to indicate an inoperable tumour.

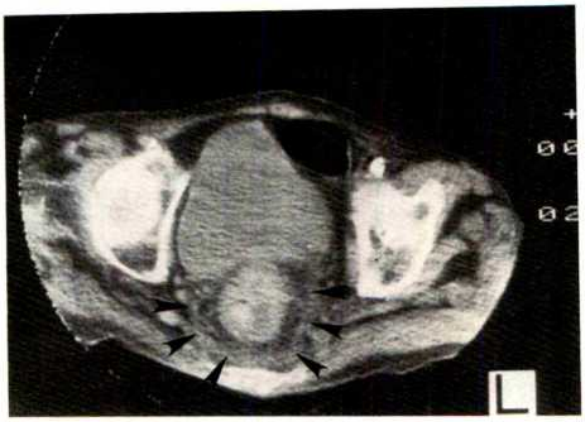


FIG. 8.

CT scan showing circumferential thickening of the perirectal fibrous tissue (arrowheads) similar to that in Fig. 7. This case was also inoperable.

In 45 of the patients in this study digital assessment of the extrarectal spread was made by up to three surgeons, each with varying experience of rectal surgery. This was part of a larger study of the clinical staging of rectal tumours, the results of which will be published elsewhere (Nicholls *et al.*, 1981). The experienced surgeon will make few major errors of interpretation and, unlike CT, he can often detect slight extrarectal spread. Both are equally accurate in identifying those patients with extensive local spread. Less experienced surgeons may be less accurate and might require CT on patients where the local spread is considered moderate or extensive on digital examination (50% of patients in this series). In this way few patients with extensive local spread should escape detection. CT should not often be required by the experienced surgeon, but even he might like confirmation of tumour bulk in those patients with extensive local spread where the resectability is uncertain. CT could be particularly useful in those patients with tumours too high for digital assessment (10% in this series). A most useful application of CT would be in the local staging of extensive tumours intended for radiotherapy and for monitoring the response to treatment. In the absence of a specimen for pathological examination the CT scan would be likely to give an objective and permanent record of the local extent in line with the pathological extent in most cases. Errors of interpretation at CT would hopefully diminish with increasing experience.

ACKNOWLEDGMENTS

We are grateful to the Trustees of St. Bartholomew's Hospital for their generosity in providing the scanner and supporting one of us (A.K.D.). EMI Medical provided clerical assistance. The various members of staff at St. Mark's and St. Bartholomew's Hospitals are thanked for their co-operation.

REFERENCES

DOUBLEDAY, L. C. and BERNARDINO, M. E., 1980. CT findings in the perirectal area following radiation therapy. *Journal of Computer Assisted Tomography*, *4*, 634–638.

KOROBKIN, M., CALLEN, P. W. and FISCH, A. E., 1979. Computed tomography of the pelvis and retroperitoneum. *Radiologic Clinics of North America*, *17* (2), 301–319.

NICHOLLS, R. J., YORK MASON, A., MORSON, B. C., DIXON, A. K. and KELSEY FRY, I., 1981. Pre-operative local staging of rectal carcinoma (in preparation).

Book review

Induced Disease—Drug, Irradiation, Occupation. Ed. by Leslie Preger, pp. xvii+399, illus., 1980 (Grune and Stratton, New York), $35.
ISBN 0-8089-1225-9

With the current rapid expansion of the pharmacopoeia and the explosion of the medico-legal aspects of induced disease, this timely publication focuses on an increasing health hazard to modern civilization.

In a successful attempt to appeal to a wide range of the medical fraternity the editor has gleaned contributions from recognized authorities on both sides of the Atlantic and produced a book which, as indicated by the title, is divided into three main sections. Each section is a compilation of detailed chapters on individual topics and the importance of detecting possible sequelae of "exposure" to these hazards, particularly to diagnostic radiologists, is obvious from the considerable number of radiographs used in the illustrations.

The section on irradiation is unduly short and limited to a discussion on the "ten day rule", radiographs taken in late pregnancy and neonatal period and the effects on the gastrointestinal tract and respiratory system. Perhaps this could have been expanded at the expense of details of the techniques of discography and epidural venography which could be gleaned from the abundant references following the chapters.

In spite of the above criticism, the fact that two isotopic illustrations have been wrongly labelled and one radiograph printed upside down, I feel this is a very useful and instructive addition for every radiological library.

J. VIRJEE.

1981, *British Journal of Radiology*, 54, 660–664

Ultrasound measurement of fetal limb lengths

By Pat Farrant, D.C.R.M.U. and Hylton B. Meire, M.B., B.S., D.M.R.D.

Department of Radiology, Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ

(*Received November 1980 and in revised form February 1981*)

ABSTRACT

The purpose of this study was to establish the normal range for measurements of fetal limb bones early in pregnancy. The results show a linear correlation between fetal biparietal diameter and limb bone length and a significant difference between the mean measurements of the individual limb bones. The clinical significance of these findings is discussed.

The purpose of this study was to see whether it is possible to diagnose or exclude the presence of limb reduction deformities, especially in the presence of lethal skeletal dysplasias and syndromes in which short limbs are associated with multiple defects such as the Ellis van Creveld Syndrome.

Measurement of limb lengths may be used as an indicator of these syndromes and if they can be reliably measured before 20 weeks gestation it may permit termination of affected pregnancies. There have recently been several reports in the literature describing limb length measurements by ultrasound (Mahoney and Hobbins, 1977; Mladinov and Krzisnik, 1977; Hobbins and Mahoney, 1980; Queenan *et al.*, 1980), all of which have quoted fairly wide normal ranges. Previous studies based on post-mortem material have also quoted wide normal ranges, since the fetal gestations have not been accurately known (Nagamori *et al.*, 1965).

We felt that it was necessary to try to establish a narrower normal range to permit the confident diagnosis or exclusion of limb shortening in cases such as those with Ellis van Creveld Syndrome where the amount of length reduction is limited.

We have therefore performed a study to establish normal ranges for the length of limb bones on patients with accurately known gestational ages and to confirm which component of the limb bone is being measured.

METHOD

A pilot study was performed on 38 patients between 16–20 weeks gestation, using a manually operated static B-scanner, and it soon became clear that a real time scanner with a frame freeze facility was necessary in order to obtain clear pictures of the whole length of the fetal limbs, which are often very mobile.

An accurate caliper system is a necessary feature of the real time system, and its accuracy should be checked with a phantom to ensure that measurements are accurate in all directions and at all magnifications.

One third of our obstetric population attend the ultrasound department for a routine ultrasound scan between 16–20 weeks of gestation, and the main study was performed on 111 of these patients.

Limb length measurements were only taken on those patients where the BPD measurement agreed with the gestation calculated from the patient's LMP to within one week; by this means errors due to gestational age uncertainty were minimized. The same method of patient selection was used in the study performed by Queenan *et al.* (1980).

We attempted to obtain three reproducible measurements on each limb bone, although it was not always possible to obtain separate measurements of each of the distal bones; in these cases just the tibia or ulna was measured. By trying to obtain reproducible measurements, errors due to movement and obliquity of the bones were minimized. Using one of the modern real time scanners (with a 3.5 MHz linear array transducer) it is usually fairly easy to recognize the separate limbs and bones within them. Each bone is scanned until the whole length is visualized. The resultant image is frozen and the

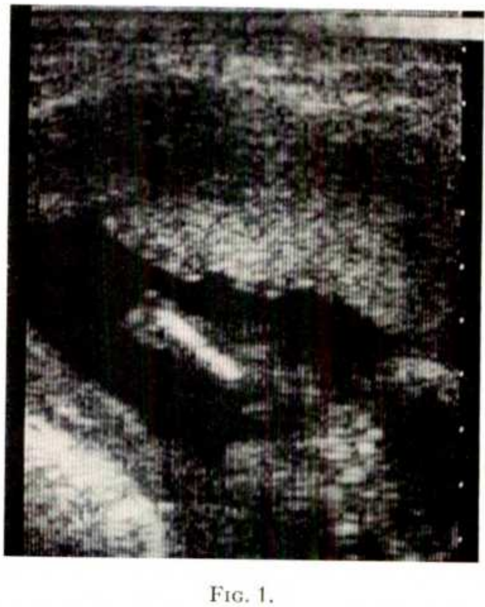


FIG. 1.

Scan demonstrating correct appearance of a humerus.

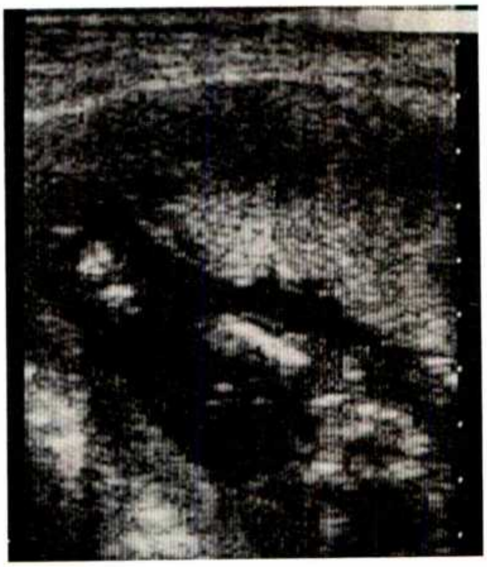


Fig. 2.

Scan demonstrating an oblique section of the same humerus.

TABLE I

Frequency of imaging the different limb bones in 111 patients

Femur	100	90%
Tibia	80	72%
Fibula	16	14%
Humerus	96	86%
Ulna	81	73%
Radius	34	31%

TABLE II

Correlation coefficients (r) for limb bone lengths with BPD and gestation calculated from LMP

	BPD	LMP
Femur	0.96	0.92
Tibia	0.96	0.94
Fibula	0.97	0.94
Humerus	0.96	0.93
Ulna	0.95	0.92
Radius	0.95	0.93

caliper markers positioned carefully on each end of the bone. The measurement obtained is noted, and the whole procedure repeated until a satisfactory, reproducible measurement is obtained. Both ends of each limb bone should appear square (Fig. 1); a pointed appearance (Fig. 2) indicates an oblique section which will result in an underestimate of bone length. Movement artefacts are easily recognized, as the image of the limb bone on the frozen picture is not the same as the real time picture seen immediately before.

As well as movement and obliquity artefacts, which are common to all the bones, there are specific errors associated with the measurement of each limb component. It is usually easiest to obtain adequate views of the femur, as its range of movements are the most limited and the pelvis and tibia are easily identified as separate structures. The tibia is more mobile and occasionally it is difficult to distinguish its lower end from the talo-calcaneal complex. We have found that the humerus was the bone of which it was most difficult to obtain adequate images. It is often difficult to differentiate the proximal end from the scapula, and if the arm is extended it may be difficult to obtain clear images of the distal end. Fetuses frequently lie in the occipito-lateral position, and one humerus is therefore in the near field of the transducer, where the resolution is relatively poor and the distal humerus lies behind the fetus and the penetration of a 3.5 MHz transducer is not adequate to obtain good quality images. The problems associated with the forearm are the same as those for the tibia.

The final measurements we accepted were not necessarily the longest or the shortest, but those we considered to fulfil all the above criteria.

Scattergrams were plotted to find out whether or not the data were normally distributed and to assess the linearity of the correlation. The data were then analysed to determine whether the limb lengths correlated better with the BPD measurement or the gestation calculated from LMP. The normal ranges for the individual limb bones were then calculated.

In order to determine if there was any difference between the mean lengths of the different bones, the means ± 2 SEMs (standard error of the mean) were calculated for each bone and the significance of the difference between the means was tested.

In order to determine which portion of the bones was being imaged we performed a small study in which the limbs of six aborted fetuses were scanned in a water bath, and X-rayed by a technique which reduced the magnification to less than 1%. The length of the ossified portion of the diaphysis was measured from the radiographs.

Results

Thirteen separate limb bones were measured on the aborted fetuses and the measurements obtained by ultrasound and X rays agreed to within 1 mm in all cases (mean error 0.54 mm).

One hundred and eleven patients entered the main portion of the trial. The frequency with which adequate measurements were obtained from the individual limb bones is shown in Table I. The scattergrams did not give any indication that the data departed significantly from normal distribution and the correlation appeared to be essentially linear. The degree of correlation between limb bone measurements and BPD or gestation from LMP was assessed by calculating the appropriate correlation coefficients (Table II). From this table it can be seen that limb bone lengths correlate more closely with BPD than with gestational age calculated from the patient's LMP. For this reason the normal ranges were calculated with respect to BPD only.

The mean values, ± 2 SEM, for the different limb bones are shown in Fig. 3. Not enough measurements were obtained from fibulae and radii to permit meaningful statistical analysis. It can be from Fig. 3A that the tibia is consistently shorter than the femur; the difference between the means is statistically highly significant for a BPD range of 30–47.5 mm ($p \ll 0.001$). The ulna is also consistently shorter than the humerus, though the difference between the means only reaches statistical significance in the BPD range of 30–42.5 mm ($p=0.046$). We also assessed the difference between the mean lengths of the femora and humeri and no significant difference was detected. The ulnae were marginally longer than the tibiae but the difference between the mean length only reached statistical significance at a BPD of 36 mm ($p=0.046$).

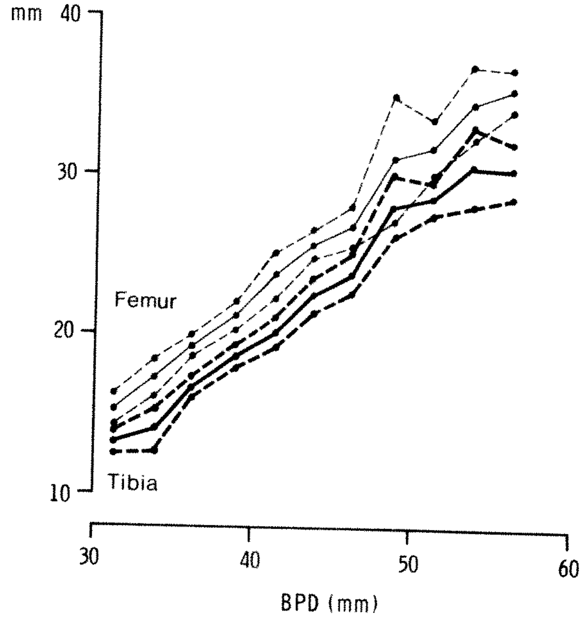
The normal ranges for femora, tibiae, humeri and ulnae are shown in Fig. 4.

Discussion

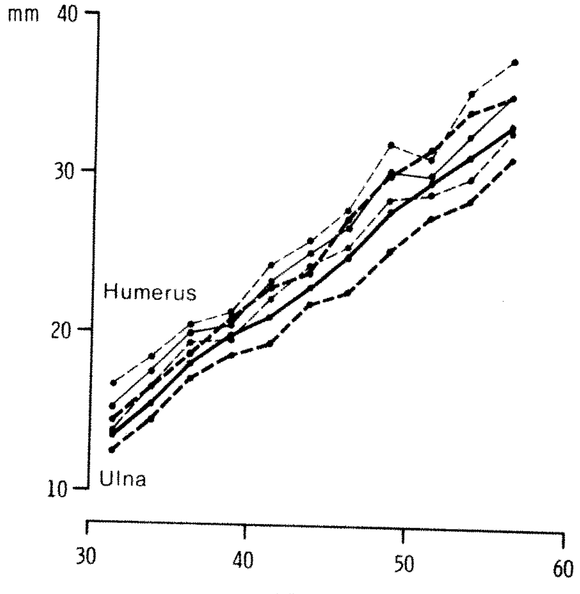
Our X-ray study confirmed that ultrasound scanning images only the ossified portion of the diaphysis. This is of particular importance when attempting to verify the ultrasound measurements by direct measurement of post-mortem material. The normal ranges quoted by Hobbins and Mahoney (1980) are based upon post-mortem measurement of whole bone lengths, and it is difficult to understand why these measurements correlate with the authors' own ultrasound measurements. Almost all other post-mortem studies have measured the length of the whole bones on fetuses of uncertain gestational age, frequently grouped in increments of one month's gestation. It is therefore essential to establish more accurate normal ranges for ultrasound measurements.

In order to obtain satisfactory measurements of limb bones, it is necessary to use a high-resolution linear-array real time scanner with a 3.5 or 5 MHz transducer, a frame freeze facility and an accurate omnidirectional caliper.

Most measurements were obtained on femora and humeri as they were less mobile than the distal limbs and it was technically easier to obtain satisfactory



A



B

Fig. 3.

Mean values ± 2 SEM for (A) femur and tibia and (B) humerus and ulna.

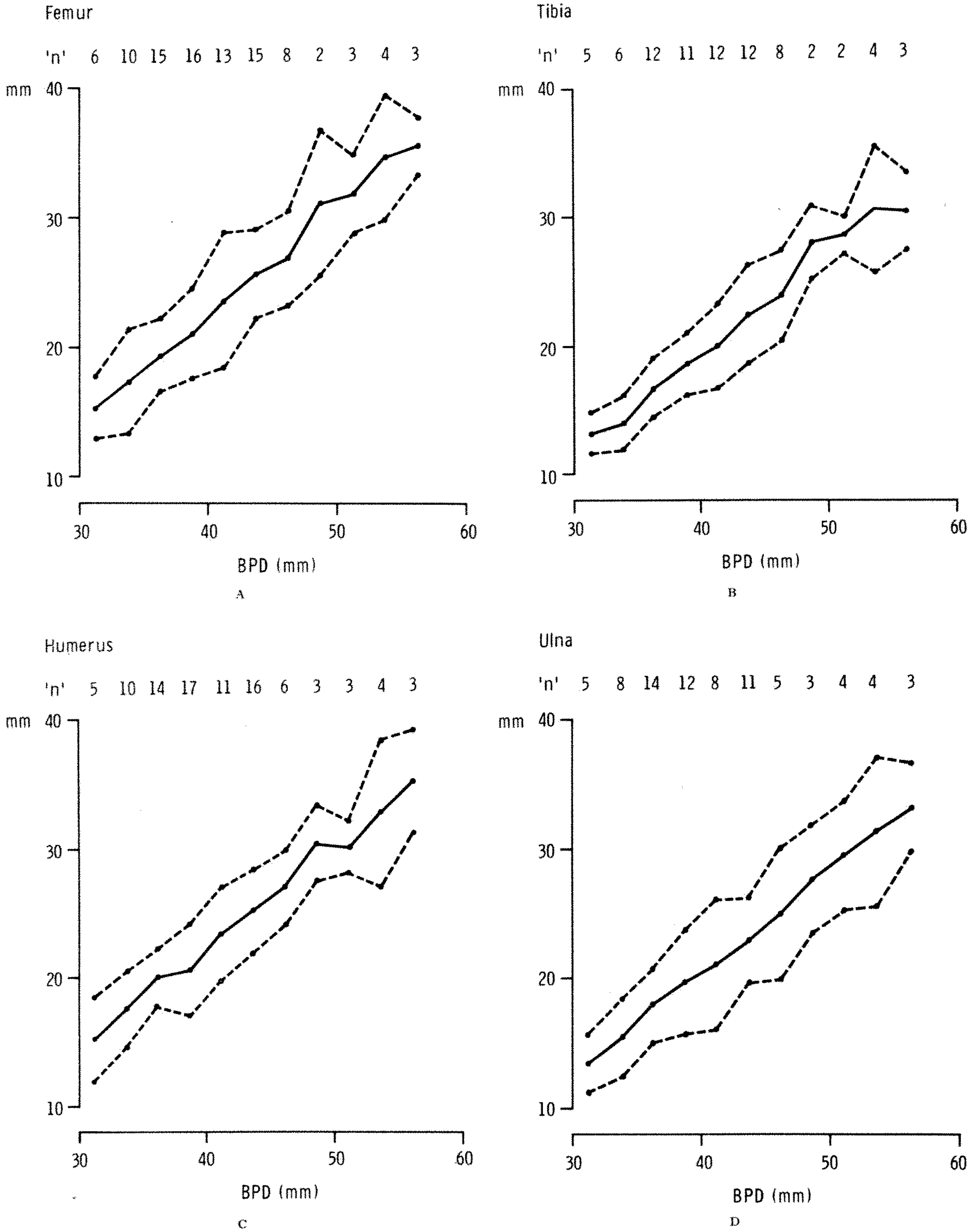


FIG. 4.

Normal ranges (± 2 SD) for (A) femur, (B) tibia, (C) humerus and (D) ulna. *n* indicates number of measurements at each interval.

images of the femur. Fewer measurements were obtained on the fibulae and radii as they are the more difficult bones to scan adequately, firstly because they are so mobile and secondly because of shadowing from the tibiae and ulnae respectively. Measurements taken before 16 weeks are technically not easy because of the small size of the fetal limbs and we have only 14 measurements taken between 15 and 16 weeks.

The decision to plot limb lengths against BPD rather than against gestation calculated from LMP clearly has a significant effect upon our normal range. In a separate study conducted in our department we found that the gestation calculated from ultrasound BPD measurement disagreed with that from LMP by more than seven days in over 14% of patients. The subsequent obstetric courses of these patients suggested that the ultrasound assessment of gestational age was more accurate than that from LMP.

Gestation calculated from LMP may contain errors due to mistaken dates, length of cycle and early or late ovulation; this therefore precludes the use of LMP-calculated gestation as the reference for limb lengths. This argument is supported by the fact that in this study the correlation coefficient for limb length against BPD was better than that for limb length against LMP.

The significant difference between the mean values for the individual limb bones indicates that separate normal ranges are necessary for each bone. If a single graph were used, a femur or humerus that was 20% shorter than normal would still fall within the normal range. The use of separate graphs would permit this amount of shortening to be detected.

REFERENCES

HOBBINS, J. C. and MAHONEY, M. J., 1980. The diagnosis of skeletal dysplasias with ultrasound. In *The Principles and Practice of Ultrasonography in Obstetrics and Gynecology.* 2nd edit. Ed. by R. C. Sanders and A. E. James (Appleton-Century-Crofts, New York).

MAHONEY, M. J. and HOBBINS, J. C., 1977. Prenatal diagnosis of chondroectodermal dysplasia (Ellis van Creveld Syndrome) with fetoscopy and ultrasound. *New England Journal of Medicine, 297,* 258–260.

MLADINOV, G. and KRZISNIK, Z., 1977. Achondroplasia revealed by ultrasound in utero. *Jugoslavenska Ginekologna i Opstetricna, 17,* 239–241.

NAGAMORI, H., EBE, M., SASAKI, M. and KURODA, S., 1965. Medico-legal studies on the fetus and the infant (II) value of the length of tubular skeletons in the estimation of the age of the fetus. *Japanese Journal of Legal Medicine, 19,* 422–430.

QUEENAN, J. T., O'BRIEN, G. D. and CAMPBELL, S., 1980. Ultrasound measurement of fetal limb bones. *American Journal of Obstetrics and Gynecology, 138,* 297–302.

Book reviews

Clinical Ultrasound Review. Vol. 1. Ed by F. Winsberg, pp. 348, 1981 (John Wiley and Sons, New York), £20.
ISBN 0-471-05738-X

This is the first in what promises to be an annual series of reviews of recent world literature on diagnostic ultrasound. Unlike many other similar reviews, this is not a collection of review articles but is compiled from a series of short abstracts of papers culled from the recent world literature. Many of the original illustrations have been reproduced and the quality of these reproductions is generally satisfactory. In addition to the abstracted text the editor has inserted his own comments at the foot of many papers and these are generally interesting and occasionally amusing.

The book is divided into four sections covering abdominal ultrasound; obstetrics, gynaecology and perinatal ultrasound; cardiac ultrasound; and Doppler. The index is satisfactory, thus enabling the reader to identify papers on the field of particular current interest, and my only major criticism is the total lack of references. The alternative style of inviting substantial review articles in such a book is probably rather less digestible but does at least give the reader a series of useful references to continue his reading should he so wish.

Despite these reservations the book can be highly recommended to all those actively involved in clinical ultrasound, since it enables one to review in a short space of time many of the significant papers published during the last year or so. With the continuing rapid increase in the number of ultrasound papers published such review books are likely to play an increasingly important role in the future and I anxiously await volume 2.

H. B. MEIRE.

An Introduction to Diagnostic Ultrasound. By Michael B. Love and Marc S. Lapavowker, 1981 (Charles C. Thomas, Springfield, Ill., USA), $18.75.
ISBN 0-398-04136-9

This short book is written with medical students in mind and illustrates some classic ultrasound findings. It is quickly read. Its claim to encompass "all recent technological advances" is rather ambitious but the physical principles are simply explained. The illustrations are "black-on-white" with adequate legends. There are some explanatory drawings. I wonder at the value of such an extensive list of references included in what is a short introduction into a subject.

Radiologists and ultrasonographers will, I believe, find it too superficial and of limited value.

A. B. AYERS.

1981, *British Journal of Radiology*, *54*, 665–670 AUGUST 1981

Ultrasonically guided percutaneous interstitial implantation of iodine 125 seeds in cancer therapy

By H. H. Holm, M.D., Ph.D., I. Strøyer, M.D., H. Hansen, M.Sc. and F. Stadil, M.D., Ph.D.

Ultrasonic Laboratory, Departments of Oncology and Gastroenterology, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark

(*Received October 1980*)

ABSTRACT

A new method for ultrasonically guided percutaneous interstitial implantation of ^{125}I seeds in abdominal tumours is described. A linear array puncture transducer mounted on a special x-y-z co-ordinate frame is used in combination with a special insertion technique. Following *in vitro* experiments the technique was applied in two patients with pancreatic cancer. There were no immediate complications after the implantation of 36 and 37 ^{125}I seeds.

Implantation of radioactive material in tumours was invented in 1901 by Pierre Curie, who used the newly-discovered radium. Since 1965 ^{125}I seeds (Fig. 1) have been used. The cylindrical seeds have dimensions of 0.8 × 4.5 mm, a half-life of 60 days and a half-value thickness in tissue and lead of 2 cm and 0.025 mm respectively. The rapid fall-off of dose from an implant consisting of 14 seeds is demonstrated in Fig. 2.

The long half-life and low energy of ^{125}I seeds have several radiobiological advantages. The radiation hazard for members of the family and for personnel is reduced to insignificant levels. The seeds are usable for long periods of time and can therefore conveniently be ordered at fixed intervals and stored until use. The seeds are usually applied as a permanent implant in the tumour.

The advantage of a ^{125}I seed implant over external radiation therapy in deep-seated cancer is the higher total tumour dose which is delivered more precisely and at a low dose rate. There is a lower dose to the normal tissue and thus a higher therapeutic ratio. Furthermore, the radiation dose is delivered and the treatment completed in one single session, as opposed to multi-fractionated external beam therapy which may take six weeks. This is of great value both from an economic and a psychological point of view.

Generally speaking, interstitial implantation is the treatment of choice for unresected cancers which are not so widespread, fast-growing or highly radiosensitive as to make external X-ray therapy or chemotherapy preferable (Hilaris, 1975).

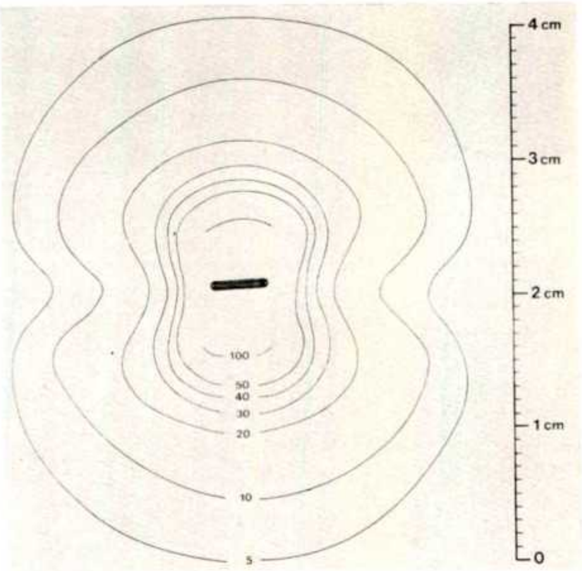


FIG. 1.
A ^{125}I seed with its dose distribution indicated.

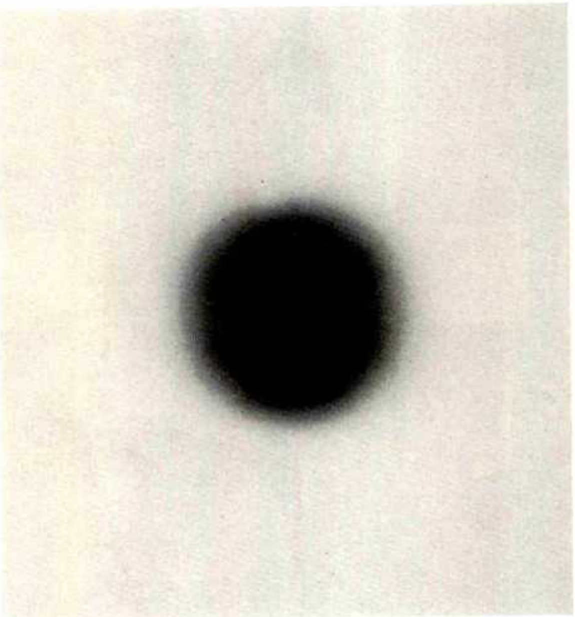


FIG. 2.
Autoradiograph of an implant consisting of 14 seeds, demonstrating rapid fall-off of dose.

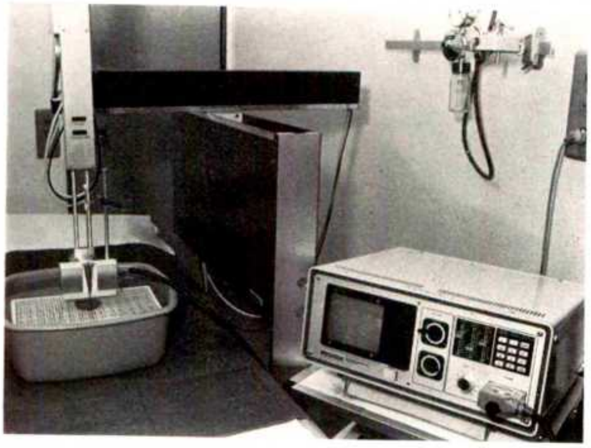


Fig. 3.

Dynamic linear-array puncture transducer mounted on an x-y-z co-ordinate system for precise ultrasonically guided needle placement. A "test tumour" is placed in a water phantom under the transducer. A needle is ready for introduction.

Implantation of ^{125}I seeds in deep-seated lesions has until now required surgical procedures. Even minor surgery must be considered a disadvantage of this technique since it adds further strain and risk to the patient. Furthermore, precise, uniform placement of the seeds is very difficult to obtain by surgical implantation.

The purpose of the present work is to describe a new technique for guided percutaneous permanent implantation of seeds.

Technique

A dynamic linear-array puncture transducer is mounted on a specially designed x-y-z co-ordinate frame which allows precise selection of a precalculated series of parallel scans through the tumour (Fig. 3). The volume of the tumour is determined on the basis of the ultrasound scans. After calculation of total activity and arrangement, a proper number of seeds spaced by small pieces of chromic catgut are

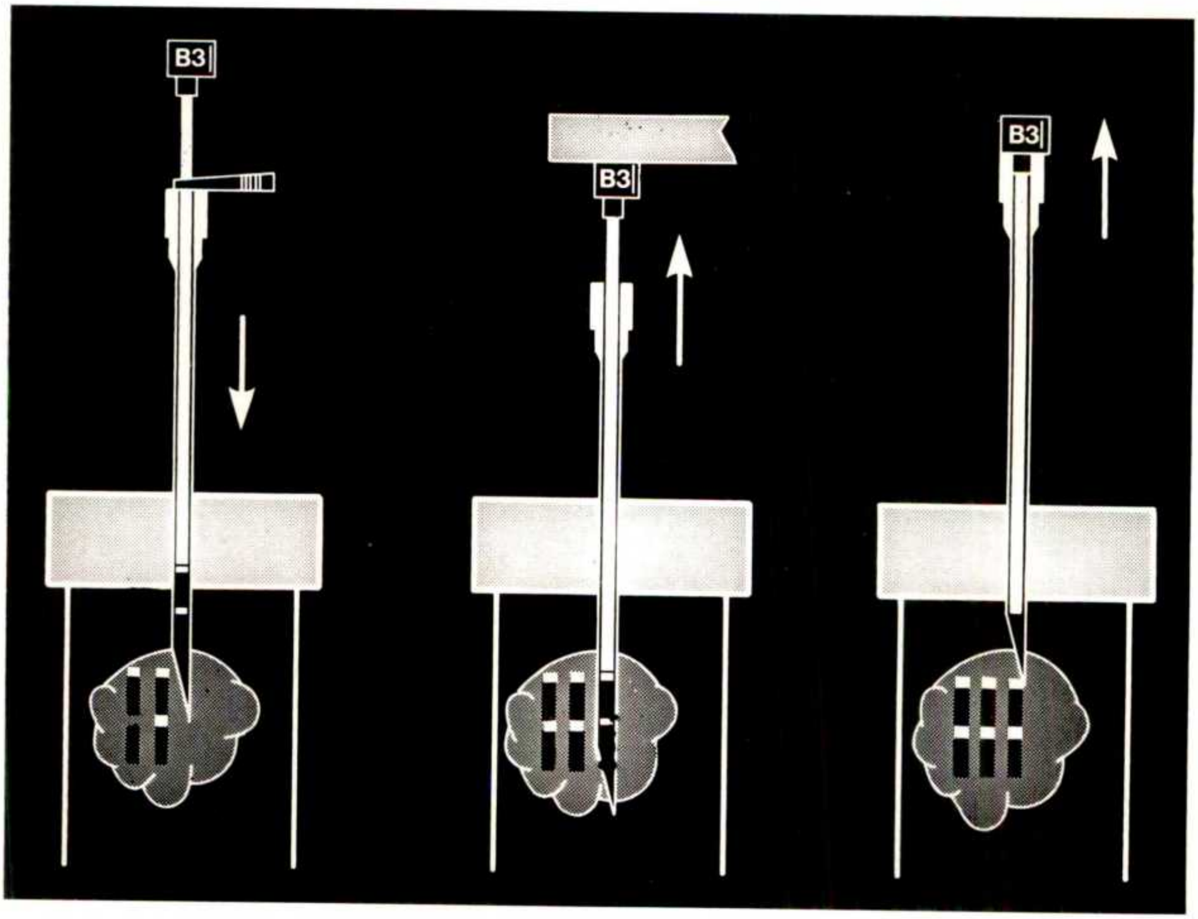


Fig. 4.

The technique of seed implantation.

loaded in a series of 1.2 mm (gauge 18) needles which have a small piece of inert silicone rubber in the needle tip to prevent the seeds from dropping out. Stylets are carefully inserted, and the needles are placed in a special shielded holder and sterilized. Guided by dynamic scanning the needle is inserted into the tumour until its tip reaches the far wall as determined by the electronic measuring device (Fig. 4). A stopper is rotated into position on top of the stylet. The needle is then withdrawn over the stylet thereby releasing the seeds inside the tumour. The needle and stylet are then removed. The pre-calculated number of needles is inserted parallel to each other in each plane, whereupon the procedure is repeated in the next parallel plane.

In vitro *experiments*

The technique has been tested *in vitro* with a 3 × 4 × 5 cm piece of liver tissue in a water phantom substituting an intra-abdominal tumour *e.g.* a pancreatic cancer (Fig. 3). A radiograph of the test tumour revealed a satisfactory, even and precise placement of the "dummy seeds" inside the test object (Fig. 5A). Figure 5B shows the test tumour transected along one of the scan planes.

Clinical application

Recently a similar procedure was carried out percutaneously in two patients with inoperable tumours in the pancreas (Fig. 6). The procedure was carried out under local anaesthesia after sedation with intravenous Stesolid®. Bleeding time and coagulation time were normal in both cases.

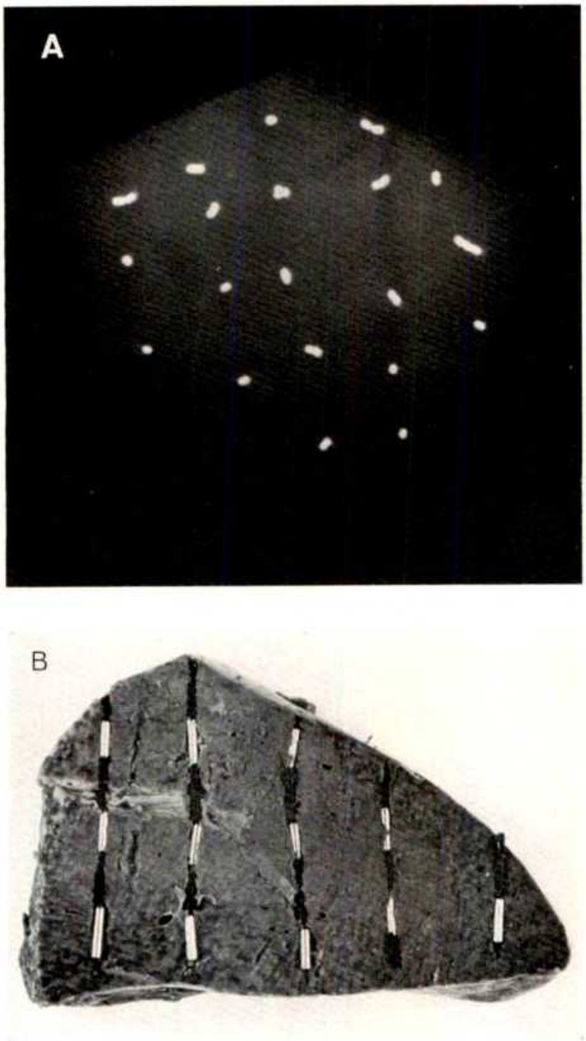


FIG. 5.

(A) Radiograph of the test tumour viewed from above. The seeds are evenly distributed in this plane.

(B) The test tumour transected along one of the scan planes. The "seeds" are seen spaced by pieces of chromic catgut.

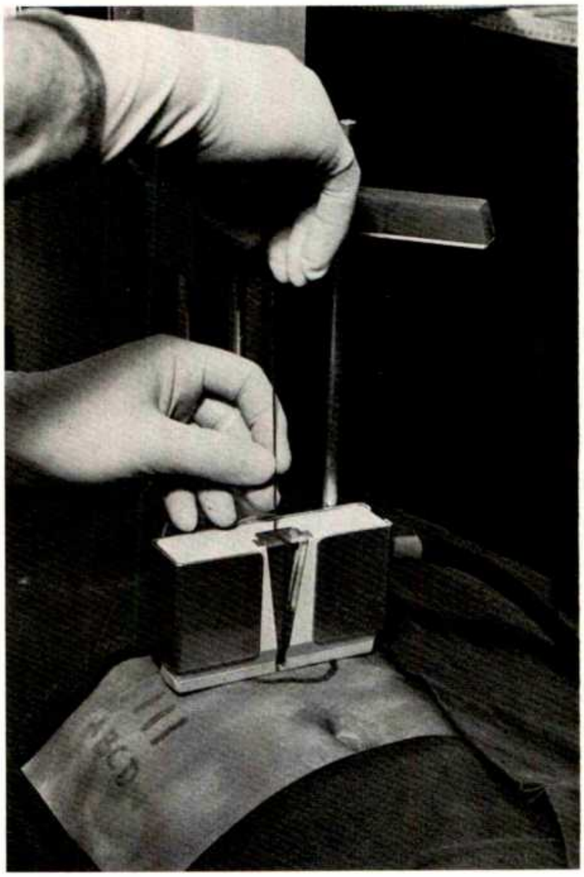


FIG. 6.

Ultrasonically-guided percutaneous interstitial implantation of ^{125}I seeds in a patient.

CASE REPORTS

Case 1

A 74-year-old woman had Verner Morrison syndrome caused by a vasoactive intestinal peptide-producing tumour in the tail of the pancreas. The tumour measured 2.5 × 3.5 × 5 cm (Fig. 7) and liver metastases were present. Ultrasonically-guided fine-needle aspiration biopsy from the tumour showed malignant cells. For three years the patient had periodically suffered from severe diarrhoea with a large loss of fluid. Cytostatic treatment and embolization of the hepatic artery had controlled the diarrhoea temporarily. Because of recurrence of watery stools it was decided to attempt interstitial radiotherapy. Under ultrasonic guidance 36 ^{125}I seeds were implanted in the deeply located tumour using eight transhepatic punctures (Fig. 8). The procedure took 20 minutes and there were no immediate complications. Radiographs in two planes of the abdomen showed that 28 seeds were located closely together, presumably inside the tumour, while eight seeds were located adjacent to the anterior part of the tumour.

The patient's diarrhoea stopped the day after the implantation and she has done well during two months' observation. A radiographic study three weeks after the implantation showed a slight shrinking of the tumour.

Case 2

A 55-year-old man had severe epigastric pain and jaundice. Percutaneous transhepatic cholangiography showed stenosis in the lower portion of the common bile duct. Ultrasonic scanning demonstrated a 3 × 4 × 5.5 cm solid lesion in the head of the pancreas (Fig. 9). An ultrasonically guided puncture from the lesion revealed malignant cells. At operation an unresectable cancer was found in the head of the pancreas. There were no liver metastases. A choledochojejunostomy was performed. Post-operatively the patient had severe epigastric pain and two weeks after surgery interstitial radiotherapy was decided upon. Thirty-seven ^{125}I seeds were implanted, using 14 ultrasonically guided percutaneous punctures. The patient experienced some pain during the procedure but no complications occurred. A radiograph showed a satisfactory distribution of all the seeds (Fig. 10).

Three days later the patient was discharged from the hospital and the tumour response will be monitored by ultrasonic scanning and plain radiography.

DISCUSSION

Interstitial radiation therapy (interstitial brachytherapy) with ^{125}I seeds has obvious advantages when compared with external radiation therapy. The optimum conditions for this kind of therapy are that the tumour should be localized and less than 7–10 cm in size, with a slow growth-rate and low to moderate radiosensitivity.

However, the use of brachytherapy in the abdomen has previously demanded surgical intervention and the technique of peroperative insertion of the

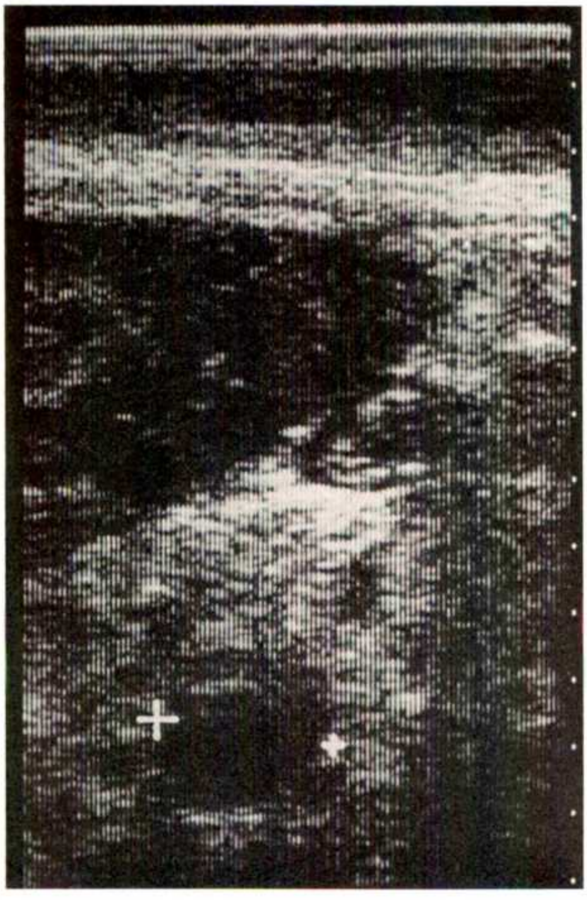


FIG. 7. *Case 1.*
Longitudinal ultrasonic scan of tumour in the tail of the pancreas.

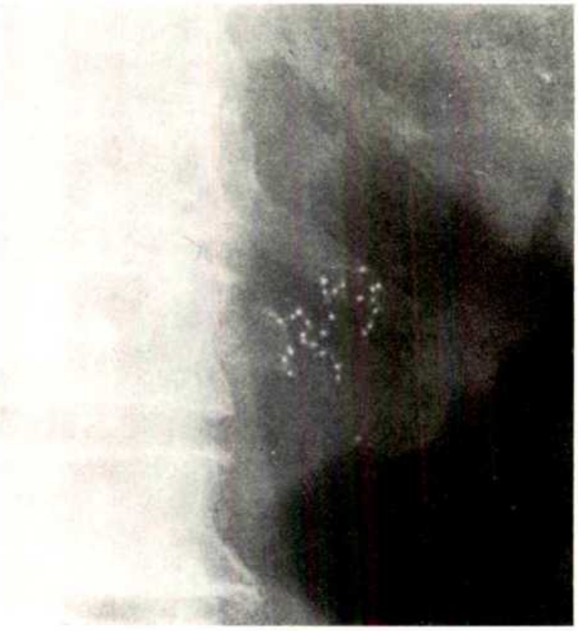


FIG. 8. *Case 1.*
Plain radiograph (AP view) with interstitial ^{125}I implantation in tumour in the tail of pancreas.

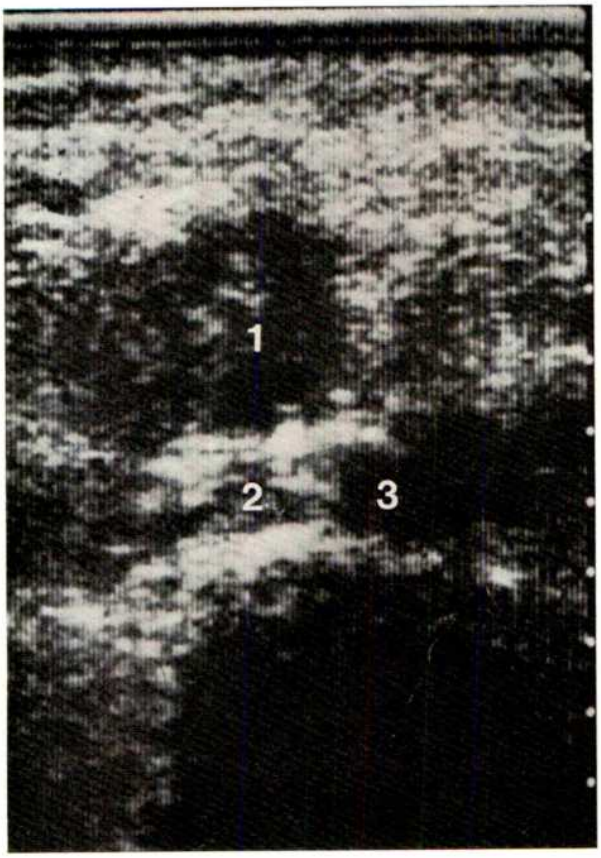


FIG. 9. *Case 2.*
Transverse ultrasonic scan of a cancer in the head of the pancreas. 1, tumour; 2, inferior vena cava; 3, aorta.

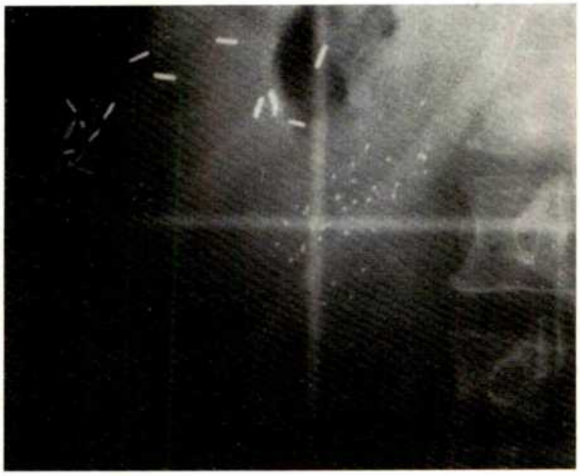


FIG. 10. *Case 2.*
Plain radiograph with interstitial ^{125}I implantation in cancer of the head of the pancreas. In the upper left corner are a number of surgical clips.

seeds is difficult. Especially in the type of cancer patients in question, it would be a definite advantage to avoid the strain of an operative procedure requiring further hospitalization. The intention of the present work has been to develop a gentle brachytherapy technique which does not require surgery.

In abdominal cases where brachytherapy is indicated, it is almost always possible by ultrasonic scanning to outline the tumour (Holm *et al.*, 1980). Furthermore, over ten years' experience with more than 3000 ultrasonically guided punctures of almost any puncture target in the abdomen has proved that this can be performed with a high degree of accuracy and almost without risk (Holm and Kristensen, 1980). These two circumstances led to the development of the present percutaneous ultrasonically-guided method for implantation of radioactive seeds in tumours, particularly in the abdomen.

It is notable, but not surprising, that no immediate complications occurred even though eight needles were introduced transhepatically in the first case and 14 through the gastrointestinal canal in the second.

The seed-implantation system which has been developed is very suitable for abdominal tumours which are not covered by ribs. Needle insertion in a cephalad angle is, however, possible to some extent. A sector scanner with puncture attachment used in combination with a co-ordinate system may prove more suitable for this purpose because its smaller contact area in some cases (*e.g.* intercostal approach) makes access easier. Furthermore, the oblique introduction of the needle into the sound field will facilitate visualization of the needle and seeds, which were not very well demonstrated with the present technique.

The percutaneous technique for implantation of seeds can also be used in conjunction with CT scanning. This, however, seems to be less suitable as a puncture guide for several reasons. It is time-consuming, the needle is not monitored during its insertion, oblique cephalad and caudad insertion is impossible, it is not a real-time technique, *i.e.* organ and target movements may cause errors, and finally it is expensive. If, however, the tumour is hidden by a gas-filled gastrointestinal tract, CT scanning can be the method of choice.

Abdominal tumours suitable for percutaneous brachytherapy may be cancers in the pancreas, the liver, the retroperitoneal space or the internal female genitalia, as well as recurrence after, *e.g.*, nephrectomy for renal cancer.

Although too much optimism is not justified for most of these patients, improved survival rates after brachytherapy have been clearly demonstrated by Hilaris (1975) in pancreatic cancer. The endocrine gastrointestinal tumours may be of particular relevance in this context because they are slow-growing and mortality is often dominated by the results of the hypersecretory states. Percutaneous implantation of radioactive seeds offers a new chance of palliation by inhibition of the excessive hormone release.

General principles in brachytherapy such as dose calculation and radiation protection are not covered in this report since they have previously been very well reviewed (Hilaris, 1975).

NOTE ADDED IN PROOF

Five additional patients have been treated using the technique described (maximum: 73 seeds/18 punctures). No complications have been registered.

REFERENCES

HILARIS, B. S., 1975 (Ed.). *Handbook of Interstitial Brachytherapy.* (Publishing Sciences Group, Acton, Mass.), p. 69.

HOLM, H. H. and KRISTENSEN, J. K., 1980 (Eds.). *Ultrasonically Guided Puncture Technique* (Munksgaard, Copenhagen).

HOLM, H. H., KRISTENSEN, J. K., RASMUSSEN, S. N., PEDERSEN, J. F., HANCKE, S., JENSEN, F., GAMMELGAARD, J. and SMITH, E. H., 1980. *Abdominal Ultrasound.* 2nd Edit. (Munksgaard, Copenhagen).

Book reviews

Ultrasonically Guided Puncture Technique. Edited by H. H. Holm and J. K. Kristensen, pp. 128, 1980 (Munksgaard, Copenhagen; Henry Kimpton, London), £11·55.
ISBN 87-16-8459-4

This is a splendid, comprehensive, compact handbook on percutaneous biopsy and imaging techniques guided and controlled by means of ultrasound. The work is based on lectures given at the well-known courses organized at Herlen Hospital in Copenhagen.

The book is full of good advice and the various techniques are well described. The risks and limitations of the methods are well discussed and the applications and results fairly presented. The illustrations are good, but labelling of the transverse scan of Fig. 1.25 has been omitted. However, the appearances are self explanatory and the pathology easily recognizable.

The scope of the book covers abdominal ultrasound anatomy and pathology, physical principles of ultrasonically guided puncture techniques, procedure, cytology, bacteriology, amniocentesis, cytochemistry and cytoimmunology. It is excellent value for £11·55 and highly recommended to all medical persons directly involved in the management of patients with ultrasonically demonstrable abnormalities of uncertain histology.

H. I. GRAVELLE.

Cases in Diagnostic Ultrasound. Vol. 1. Ed. by George R. Leopold, pp. 206, 244 ill., 1980 (John Wiley & Sons, New York/Chichester/Brisbane/Toronto), £13·50.
ISBN 0-471087319

For the last five years, the Los Angeles Radiological Society has held a Spring Diagnostic Ultrasound Conference. This has proved to be very popular. Small group discussions led by nationally prominent and local ultrasonographers and centred around cases in the workshop syllabus are a feature of the Conference. This volume records the workshop syllabus for the 5th conference, selected to provide a comprehensive and current overview of the field of diagnostic ultrasonic imaging. The original group discussion which took place when each case was presented is left to the imagination of the reader. A very brief history of each case is given on one page together with the illustrations of the chosen ultrasonic scans. Over the page is a short description of the scans, a discussion and the diagnosis. Each case is accompanied by a relevant bibliography which is an excellent feature of the text. The cases are divided into six chapters on basic abdominal, basic obstetrics and gynaecology, liver and biliary tract, pancreas and spleen, retroperitoneum and kidney, and finally advanced obstetrics and gynaecology, each compiled by a different contributor. The cases are well chosen to illustrate the simple, the not so simple through to the exotic. The range is wide, 105 cases being presented. The quality of the illustrations is excellent if allowance can be made for the frequent confusion inherent in publications from the USA in which some illustrations are printed positive and others negative. A sound knowledge of ultrasonic interpretation is assumed, the reader having to rely on his/her skill to see the features in the illustrations which are described in the text. The discussion on each case is generally adequate and relevant and correlation with other diagnostic methods is considered, albeit superficially.

Most readers will find these cases interesting and instructive. It is the reviewer's opinion, though, that this publication is more suited to the departmental or hospital library than the individual radiologist's personal library.

F. G. M. ROSS.

1981, *British Journal of Radiology*, 54, 671–673 AUGUST 1981

Technical notes

A catheter system for the safe and efficient delivery of tissue glues (bucrylate) for visceral embolization

By M. S. Khangure, M.R.C.P. (UK), F.R.C.R., M.R.A.C.R., H. T. ApSimon, F.R.C.R., F.R.A.C.R., T. M. H. Chakera, M.R.C.P., F.R.C.R., F.R.A.C.R. and D. E. Hartley, F.I.R., M.A.S.X.T.

Department of Diagnostic Radiology, Royal Perth Hospital, Wellington Street, Perth, Western Australia

(Received December 1980 and in revised form April 1981)

A number of different materials are used for trans-catheter embolization because no single substance is suitable for all situations (Berenstein and Krischeff, 1979). In general, it should be possible to control the depth of vessel penetration and to avoid remote embolization or reflux. The material should have low histo-toxicity and be easy to deliver. In addition, liquid emboli need to have low viscosity to pass easily through fine catheters; to be radio-opaque, produce permanent occlusion, have a short setting time and not adhere to the delivery catheters.

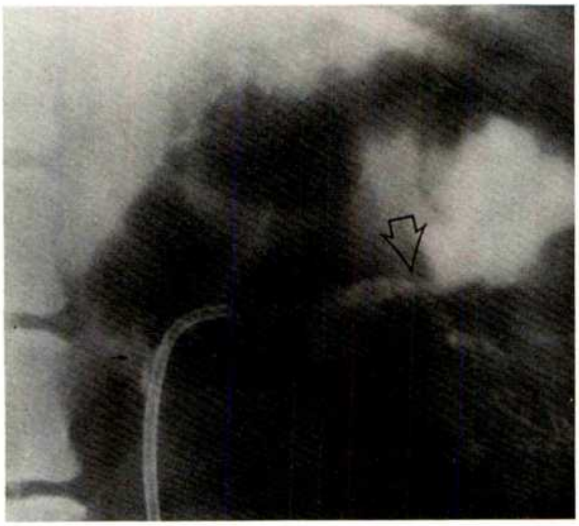


FIG. 1.

Opacified bucrylate was injected through a coaxial catheter without flow control. The catheter tip was placed in a segmental renal artery well beyond the division of the main renal artery (large open arrow). Opacified bucrylate is shown in almost the entire length of the main renal artery (vertical arrows) and in the abdominal aorta around the guiding catheter (horizontal arrows). Reflux embolization was observed on several occasions when no flow control was used.

Bucrylate (isobutylcyanoacrylate) fulfils, or can be made to fulfil, these conditions. As it is difficult to handle, preliminary laboratory and animal studies are essential. Complications are caused by reflux of emboli or excessive penetration of the capillary bed (White *et al.*, 1977; Greenfield *et al.*, 1978; *Lancet* editorial, 1978). Our animal study shows that circulatory flow control is highly desirable when using liquid emboli (Fig. 1).

MATERIALS AND METHODS

We used a circulatory model to show that a 1:1 v/v suspension of bucrylate and Pantopaque (iophendlate) is suitable for trans-catheter embolization. This suspension is homogeneous and stable and sufficiently opaque to be visualized on fluoroscopy, and its viscosity is low enough for delivery through fine catheters. Pantopaque facilitates the delivery of bucrylate by retarding its polymerization (Cromwell and Kerber, 1979).

A catheter system (Fig. 3) was designed incorporating a balloon for flow control, and was assessed using the renal and visceral vessels of dogs. The system consists of a thin flexible double lumen balloon catheter which is coaxially introduced through a preshaped polyethylene guiding catheter. The coaxial balloon catheter unit (Fig. 2) is 80 cm

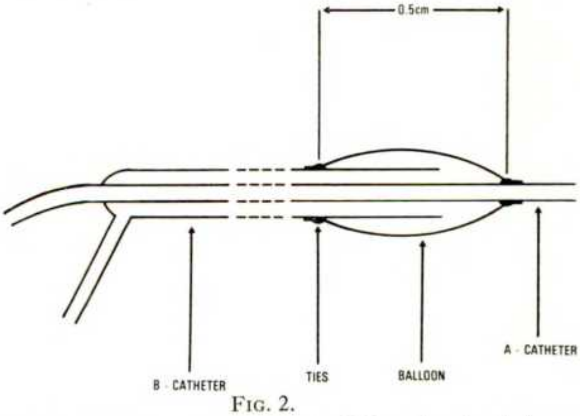


FIG. 2.

Balloon catheter unit. Catheter A: 1 French polyethylene; Catheter B: 3 French Teflon tubing.

This publication is based on a paper presented at the 31st Annual General Meeting of the Royal Australasian College of Radiologists in October, 1980.

Address for reprints: Dr. T. M. H. Chakera, Department of Diagnostic Radiology, Royal Perth Hospital, Box X2213, G.P.O. Perth, WA 6001, Australia.

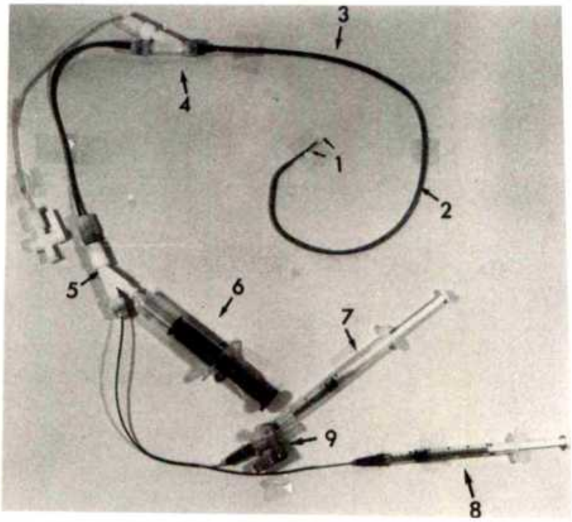


FIG. 3.

Assembled catheter arrangement. (1) The balloon and tip of balloon catheter unit introduced coaxially through the guiding catheter. (2) The guiding catheter. (3) Teflon introducer sheath. (4) Y connector attached to introducer sheath. The straight limb allows the introduction of the guiding catheter. The side arm is used to flush the sheath intermittently with heparinized saline. (5) Y connector attached to the end of the guiding catheter. The straight limb is used for the introduction of the balloon catheter unit. The side arm is used for the intermittent perfusion of heparinized saline into the guiding catheter. (6) 1 ml syringe containing contrast medium for balloon catheter. (7) 1 ml syringe containing opacified bucrylate. (8) Two way tap used to keep balloon inflated.

long and consists of an inner 1 French polyethylene tube inserted through an outer 3 French Teflon tube. The balloon is formed by a short length of 0.12 mm diameter medical-grade silicone tubing, one end attached to the polyethylene and the other end to the Teflon. The clearance between the catheters provides a lumen for the control of balloon inflation. The inner catheter is used for test injections of contrast media and for the delivery of tissue glues. The preshaped guiding catheter, through which the balloon catheter unit is introduced, is 6.5 French polyethylene. It can be readily steamed over a forming wire into any desired shape. A Teflon sheath (Cook) is used to facilitate a rapid exchange of the guiding catheters. Before the balloon catheter unit is introduced, the lumen of the 3 French Teflon catheter is filled with Conray 420, to get rid of air bubbles which might burst the balloon. The silicone balloon and catheter tip are lubricated with silicone fluid to prevent the bucrylate from sticking to the balloon.

The bucrylate/Pantopaque suspension is prepared in the 1 ml syringe. All air is expelled from the syringe after the Pantopaque has been drawn up; the drawing-up needle is filled with Pantopaque before drawing up the bucrylate to ensure that no residual air is left in the syringe, so preventing any loss of bucrylate in attempting to eliminate air. Protective goggles and gloves are worn at all stages when using bucrylate, because if the syringe is disconnected from the catheter while injecting the suspension the bucrylate squirts everywhere. The chance of accidental disconnection when using fine catheters can be much reduced by first rehearsing injection with Pantopaque before attempting it with bucrylate.

The femoral artery of an anaesthetized dog is dissected and punctured under direct vision using a modified Seldinger technique. A 6.5 French Teflon introducer sheath (Cook) is then inserted. The tip of the guiding catheter is placed in the origin of the artery, by the usual catheterization techniques. The balloon catheter is now introduced through the guiding catheter. By a combination of catheter manipulation and partial balloon inflation, the balloon catheter is advanced until the catheter is in the right place. The balloon is inflated to achieve flow control. A measured volume of contrast medium is then injected through the lumen of the 1 French tubing; the degree of vascular filling produced is assessed fluoroscopically and the volume of bucrylate needed to penetrate the vessel satisfactorily is measured.

After deflating the balloon, and irrigating the lumen of the 1 French tubing with heparinized saline, the lumen is irrigated and left filled with 5% dextrose. This ensures that the catheter lumen, through which the bucrylate is to be injected, is purged free of all ionic material (blood, contrast medium, saline). The balloon is now reinflated and the volume of opacified bucrylate, equal to the sum of the dead volume of the catheter and measured volume, injected. The balloon is deflated and the catheter unit removed after radiography. The embolized kidney and main renal artery are removed and radiographed on fine detail film. Any reflux embolization and the degree of vascular penetration are easily assessed. Further examples of segmental renal artery embolization, main renal artery embolization and visceral artery embolization are shown in Figs. 4 and 5.

RESULTS

A total of 16 renal arteries and eight visceral arteries have been embolized. No catheter has glued *in situ* and no reflux embolization has taken place.

Histological study has demonstrated intra-arterial placement of the bucrylate when flow control is used.

1981, *British Journal of Radiology*, 54, 673–677 AUGUST 1981

Technical notes

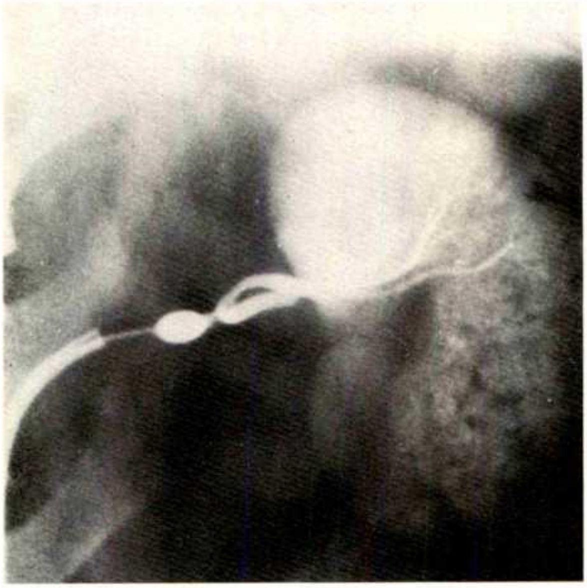


FIG. 4.

Opacified bucrylate is shown in the upper pole renal arteries. The balloon, inflated with contrast medium, is shown *in situ*, preventing any reflux embolization.

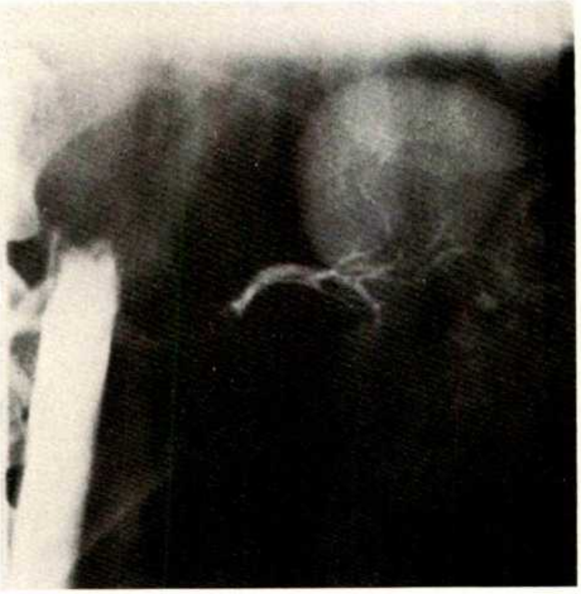


FIG. 5.

The main renal artery has been embolized with opacified bucrylate and the balloon catheter unit has been removed. Bucrylate is shown in the distal main renal artery and some segmental branches. The flush aortogram demonstrates the origin and proximal segment of the renal artery to be patent.

Without flow control, the presence of tissue glue in glomerular capillaries and venules is evident, indicating excessive vascular penetration.

On several occasions the balloon catheter was deliberately glued *in situ* by not lubricating the balloon and injecting excessive amount of tissue glue. In this situation the catheter unit is easily removed by hyperinflating and rupturing the balloon, thus leaving a portion of the silicone balloon *in situ*. No vascular rupture was detected on subsequent dissection of the vessels.

ACKNOWLEDGMENTS

We wish to thank the Department of Diagnostic Radiology Trust Fund of Royal Perth Hospital for funds made available for this project, the members of the Research Centre for assistance and the Pathology Department for the histological studies. Our thanks also to Mrs. S. Mathie for typing the manuscript.

REFERENCES

BERENSTEIN, A. and KRISCHEFF, I. I., 1979. Catheter and materials selection for trans-catheter embolisation. Technical considerations. *Radiology*, *132*, 631–639.

CROMWELL, D. C. and KERBER, C. W., 1979. Modification of cyanacrylate for therapeutic embolisation. *American Journal of Roentgenology*, *132*, 799–801.

GREENFIELD, A. J., ATHANASOULIS, C. A., WALTMAN, A. C. and LE MOURE, E. R., 1978. Transcatheter embolisation: prevention of emboli reflux using balloon catheters. *American Journal of Roentgenology*, *131*, 651–655.

EDITORIAL, 1978. Therapeutic Embolisation. *Lancet*, *i*, 1135–1136.

WHITE, R. I., JR., STRANDBERG, J. V., GROSS, G. S. and BARTH, K. H., 1977. Therapeutic embolisation with long term occluding agents and their effects on embolised tissues. *Radiology*, *125*, 677–687.

Longitudinal emission tomographic imaging using a three-pinhole aperture and an Anger camera

By S. Webb, Ph.D., D.I.C., A.R.C.S.

Physics Department, Institute of Cancer Research and Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT

(Received September 1980 and in revised form December 1980)

Single-photon emission tomographic imaging subdivides into two classes of technique: transverse-section computed tomography and longitudinal-section tomography. Longitudinal tomography can be achieved by combining a gamma camera with a spatially or time coded aperture or with a segmented multiple-pinhole collimator (Budinger, 1980). Longitudinal imaging using the latter type of collimator generates spatially distinct camera images. The reconstruction of longitudinal sections from such non-overlapping images does not necessitate decoding of an aperture function. Instead, reconstruction proceeds by iteration and, in principle, provided criteria for depth resolution are met, complete decoupling of reconstructed planes (blur-free imaging) results. For identifying lesions the absence of blurring artefacts is a great advantage over coded aperture imaging in which it is difficult to completely decouple planes (Webb *et al.*, 1978); additionally, multiple-pinhole tomography can quantitatively map out the uptake of a radionuclide in organs and tumours. To date several workers, notably including Vogel *et al.* (1978, 1979), have concentrated on the development and application of a seven-pinhole aperture for myocardial imaging. Limited by a very small field of view, the seven-pinhole aperture has not found wider application in nuclear medicine. In this note an imaging technique based on the use of an aperture comprising three pinholes arranged in a triangle is proposed which overcomes this limitation and can lead directly to an extension of quantitative, completely decoupled, longitudinal tomography into other important fields of nuclear medicine.

In this note the physical reasons underlying this choice of multi-pinhole aperture are presented and its imaging characteristics are described. An aperture is in course of construction and experimental results will be presented in a future paper.

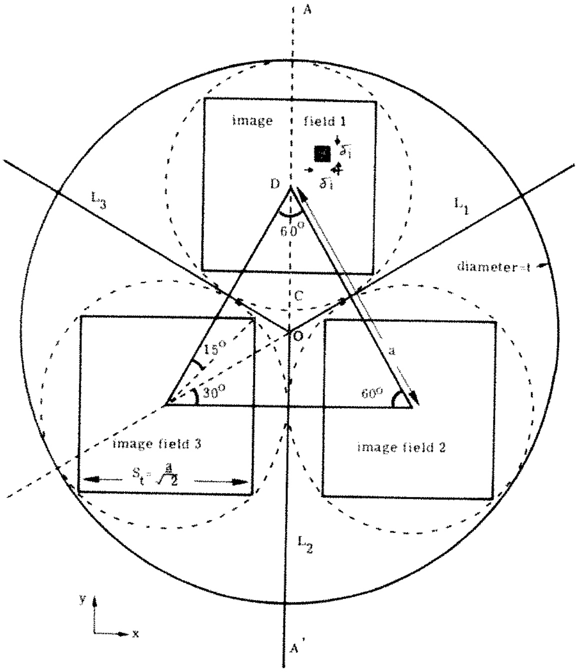


FIG. 1.

Three circular image fields tessellated on the camera plane. Symbols are defined in section 2. L_1, L_2, L_3 are positions of lead dividers to exclude any scattered radiation.

SELECTION OF THREE-PINHOLE APERTURE

The number N of pinholes and their geometric arrangement on an aperture plate is governed by the tessellation of the N distinct image fields within the sensitive circular crystal area of the gamma camera. For example, three pinholes arranged on an equilateral triangle and separated from each other by a distance w on the aperture plate enable three circular image fields to be tessellated on the crystal face as shown in Fig. 1. The centres of these fields, being the images of an axial point source at a depth P_1 below the aperture plate, are separated by a distance a. Three square image fields whose sides are

$$S_t=a/\sqrt{2} \quad . \quad . \quad . \quad . \quad . \qquad (1)$$

are fitted within the circular image fields for convenience of (x, y) digitization. The projections of the three square image fields through the pinholes all overlap at depth P_1 to define a square field of view of area F^2 where

$$F=\frac{aP_1}{v\sqrt{2}}=\frac{S_tP_1}{v} \quad . \quad . \quad . \quad . \quad . \qquad (2)$$

and v is the distance between the aperture plate and the face of the sensitive crystal (Fig. 2). Simple geometry shows that the diameter, t, of the sensitive circular crystal area is related to a by

$$t=(1+2\sqrt{3})a=2.15a \quad . \quad . \quad . \qquad (3)$$

and that

$$w=\frac{aP_1}{P_1+v} \quad . \quad . \quad . \quad . \quad . \quad . \qquad (4)$$

The fraction f_A of crystal area occupied by the three square image fields is

$$f_A=\frac{4}{\pi t^2}3S_t^2=\frac{6}{\pi}\left(\frac{a}{t}\right)^2=0.41 \quad . \quad . \quad . \qquad (5)$$

Similar diagrams to Fig. 1 have been drawn for the image fields corresponding to four pinholes arranged on a square, five pinholes on a pentagon, six pinholes on a hexagon and eight pinholes on an octagon. In the latter two cases an additional central axial pinhole will generate an image field which can be fitted inside the other six or eight fields. Hence such seven and nine-pinhole apertures make unnecessary a consideration of the corresponding six and eight-pinhole apertures without the central hole. The seven-pinhole aperture is available commercially from several companies. For each of the above five

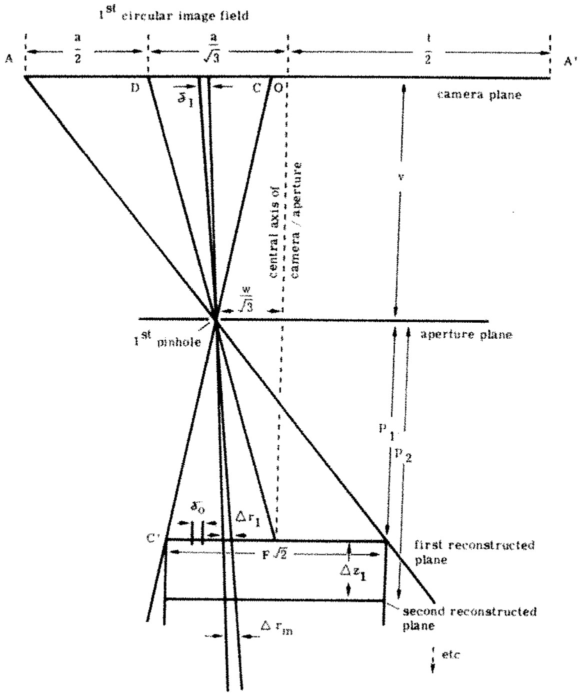


FIG. 2.

Vertical section through AA^1 in Fig. 1 indicating geometrical relationships between image and object fields. The square image and object fields are fitted inside the circular fields shown. Symbols are defined in section 2.

apertures the relationship between *a* and *t* was established geometrically and is, of course, different from that in equation (3) for the three-pinhole aperture. (For the two apertures with a central hole, *a* means the width between images of those pinholes on the vertices of the appropriate polygon). Equations (1), (2) and (4) are equally valid for these other apertures. In particular it is clear from equation (2) that both the areas of each image field and the area of the field-of-view are proportional to S_t^2. Table I lists the ratio t/a, the value of S_t^2 and the fractional crystal area utilised f_A for the five multi-pinhole apertures considered.

It is clear from Table I that as the number of pinholes decreases the field of view of the camera increases. For example, the area of the field of view for a three-pinhole aperture is 1.93 times that of a seven-pinhole aperture for the same total crystal area (same t) and same geometrical configuration (same P_1 and v). In addition, provided the object to be imaged fills the field of view, the sensitivity of the camera is for any fixed distance of the object from the aperture is proportional to f_A, the fraction of crystal area utilized, and not to the number of aperture pinholes. Hence with the three-pinhole aperture the camera is only 0.83 times as sensitive as with the seven-pinhole aperture and this small loss of sensitivity is not serious. Of course when imaging an object smaller than or equal in size to the field of view defined by the seven-pinhole aperture for example, the camera with the three-pinhole aperture would be only 3/7 times as sensitive as the camera with the seven-pinhole aperture. Since it is for large-field tomographic imaging that the three-pinhole aperture is being developed, this situation does not arise.

The purpose of reconstruction is to generate M longitudinal square planes (object fields) of area F^2 at depths $P_1, P_2 \ldots P_m \ldots P_M$ from three image fields on the camera such that the M planes span the emitting volume. The image fields are digitized into square pixels of area δ_I^2 and the object fields are reconstructed digitally using square pixels of area δ_0^2. For pinholes considered to be mathematical points the planar resolution Δr_m and depth resolution Δz_m increase with depth and are dependent on the size of the camera image pixels.* For pinholes of finite size encountered in practice these resolutions will be degraded somewhat and will depend also on the pinhole diameter. The effect of a pinhole of finite diameter is to blur out information on the camera image. This blurring may have a more marked effect on resolution than that introduced by detector pixels of finite size.

TABLE I

Number of pinholes (N)	Camera diameter ÷ diameter of each image field (t/a)	Size of each image field (S_t^2)	Fraction of crystal area used for imaging (f_A)
3	2.15	$0.108t^2$	0.41
4	2.41	$0.086t^2$	0.44
5	2.70	$0.069t^2$	0.44
7	3.00	$0.056t^2$	0.50
9	3.61	$0.038t^2$	0.44

Geometrically established parameters for N-pinhole camera apertures.

---

*Idealized formulae and proofs available on request.

When reconstructing from projections the question arises of whether there are enough projection data to determine the desired reconstruction solutions. An application of information theory indicates that, subject to the geometric criterion*

$$\frac{t}{\delta_I(1+P_1/v)} < 94.7 \quad . \quad . \quad . \quad . \quad (6)$$

three angle reconstruction tomography is overdetermined. Since t and δ_I are determined by the camera, this reduces to a condition on v/P_1 which is satisfied by practical values of P_1 and v. Hence the reconstruction of M longitudinal planes from just three views is overdetermined.

THE RECONSTRUCTION ALGORITHM

The reconstruction technique is a composite of the two techniques reported by Vogel *et al.* (1978, 1979). The three image fields may be imagined to be back-projected through the three pinholes into the object space extending downwards to infinity. For each of the M object planes, the contribution to each pixel in each plane from the three image fields was determined by intersection. These contributions were weighted by the factor $e^{-\mu h_{ijm}}$ to compensate for attenuation where h_{ijm} is the tissue path length between each (i, j, m)th object pixel and the corresponding aperture pinhole and μ is the narrow-beam linear attenuation coefficient of the radiation. Scatter rejection is assumed to be achieved electronically in the camera. The three contributions thus weighted were then added reciprocally for each and every object pixel and re-inverted to give a first estimate of the M planes. Reciprocal addition is a useful tool for generating the first estimate since if any image pixel is empty it is known and mathematically established immediately that all object pixels connecting geometrically to this image pixel are zero.

The first estimate does not represent the true object distribution, however, and must be refined iteratively. The three images of the M first estimate object planes are formed including a weighting $e^{-\mu h_{ijm}}$ to account for attenuation. Subsequently the differences between these pseudo-image fields and the true image fields are determined.

From the "difference image fields", "difference object planes" are reconstructed as above by geometrically linking object planes and image fields except that the contributions to these "difference object planes" are formed by direct addition rather than by reciprocal addition. A fraction r of the M "difference object planes" is then added to the first estimate of the M object planes to establish the second estimate of the M object planes. The technique then cycles iteratively. The fraction r of the difference object fields is termed the relaxation constant and the speed of convergence depends on the degree of relaxation.

RESULTS FROM A COMPUTER SIMULATION OF THE IMAGING MODALITY AND SUBSEQUENT RECONSTRUCTION

In order to demonstrate that three-angle reconstruction tomography can indeed yield quantitative sectional data the reconstruction technique described above was modelled computationally. The model indicates how well reconstruction can take place from noisy image data and what relaxation r should be applied. The latter is inherently related to the number of iterations performed. Clearly, if r is very close to zero a very large number of iterations will be necessary for convergence, even with noiseless data. Vogel *et al.* (1978) indicate that about 10 iterations are necessary with experimental image data but do not discuss relaxation; albeit the reconstruction techniques they describe are also somewhat different. The speed of the technique described here is approximately 1 s per iteration cycle using a CDC 7600 computer and a Fortran 4 coding.

The relaxation constant

Four planes at depths 15, 17, 19 and 21 cm were reconstructed from simulated images of point sources of activity in a background with a source to background ratio of 2. The activity was assumed to lie only in these planes. The camera parameters were $t=32$ cm, $\delta_I=0.2$ cm, $v=12.7$ cm.

The optimum choice of relaxation constant r was determined by investigating the mean $\bar{b}$ and standard deviation σ_b of the reconstructed data after 100 iterations. These data for the plane at depth 15 cm reconstructed from noiseless images are shown in Table IIA. For values of $r<0.1$ the iterative reconstruction monotonically converges with the speed of convergence decreasing as r decreases. For values of r larger than about 0.1 the iterations rapidly diverge, however. Hence the choice of $r\approx 0.1$ is a compromise between the need to optimize speed of convergence and the need to preserve that convergence and avoid divergence. Similar conclusions arise from inspecting the data in the other three planes. Additionally, inspection of the entire reconstructed field indicates that reconstructions after 100 iterations with $r=0.1$ are quantitatively almost identical (rms standard deviation closer to its true

---

*Proof available on request.

TABLE II

(A) Noiseless image data			(B) Image data comprising 10^6 photons	
Relaxation constant (r)	Mean in plane 1 ($\bar{b}$)	Standard deviation in plane 1 σ_b	Mean in plane 1 ($\bar{b}$)	Standard deviation in plane 1 σ_b
0.01	0.4938*	0.026 57	0.4949†	0.038 48
0.02	0.4976*	0.021 60	0.4988†	0.035 88
0.04	0.4998*	0.019 61	0.5011†	0.035 31
0.10	0.5007*	0.019 23	0.5020†	0.035 64
0.3	‡		‡	
0.5	‡		‡	
True object data	0.5007	0.019 22		

Reconstruction of distributions of point sources of activity from simulated images, showing the need to choose the relaxation constant correctly.
*Convergence at all cycles.
†Initial convergence followed by weak divergence.
‡Rapid divergence.

value than 0.1%) to the simulated object. If less accurate reconstructions were acceptable the number of iterations could be correspondingly reduced. Vogel *et al.* (1978) have suggested, for example, that iterations might be terminated after a 90% reduction in σ_b from its value at the first iteration.

In the presence of noise in the image field the reconstructions initially converge with $r < 0.1$ and then diverge very slowly. Table IIB presents the corresponding results. Again a relaxation constant of the order of 0.1 gives the fastest convergence. For reconstruction from a noisy image the suggested technique is to terminate iteration as soon as the weak divergence begins. The iterative reconstruction technique establishes the mean accurately but clearly will not reconstruct the correct standard deviation because of noise propagation back into the object field.

Dependence of reconstruction on noise

For the same geometrical parameters and simulated object, the behaviour of relaxed reconstruction (with $r=0.1$) was determined with varying noise contributions in the image. Table III shows the mean $\bar{b}$ and standard deviation σ_b of the data in plane 1 after 100 cycles of iteration. As anticipated the reconstruction has a higher standard deviation as the noise in the image fields increases. Again the mean is fairly accurately recovered. The behaviour in other planes is similar and by inspecting the entire set of reconstructed planes it is clear that serious artefacts arise only if the number of detected photons is much less than 10^6.

TABLE III

Number of recorded photons in image	Mean in plane 1 ($\bar{b}$)	Standard deviation in plane 1 (σ_b)
∞	0.5007	0.019 23
5×10^6	0.5013	0.023 70
10^6	0.5020	0.035 64
5×10^5	0.5025	0.046 30
10^5	0.5049	0.095 23

Reconstruction of distributions of point sources of activity from simulated images showing the effect of noise in the image (results are for 100 iterations and relaxation $r=0.1$).

CONCLUSION

The choice of a three-pinhole aperture for large field tomographic imaging in oncology has been justified in terms of its field of view and sensitivity and the reconstruction technique has been validated by means of a computer model simulating noisy data. Such an aperture has been constructed at the Royal Marsden Hospital, Sutton and its use is currently being evaluated.

ACKNOWLEDGMENT

I am grateful to Mrs. M. Flower for discussion during the preparation of this manuscript.

REFERENCES

Budinger, T. F., 1980. Physical attributes of single photon tomography, *Journal of Nuclear Medicine*, *21*, 579–592.

Vogel, R. A., Kirch, D. L., Le Free, M. T. and Steele, P., 1978. A new method of multiplanar emission tomography using a seven-pinhole collimator and an Anger scintillation camera. *Journal of Nuclear Medicine*, *19*, 648–654.

Vogel, R. A., Kirch, D. L., Le Free, M. T., Rainwater, J. O., Jensen, D. P. and Steele, P., 1979. Thallium-201 myocardial perfusion scintigraphy; results of standard and multi-pinhole tomographic techniques. *American Journal of Cardiology*, *43*, 787–793.

Webb, S., Parker, R. P., Dance, D. R. and Nicholas, A., 1978. A computer simulation study for the digital processing of longitudinal tomograms obtained with a zone plate camera. *IEEE Transactions on Biomedical Engineering*, *BME-25*, *2*, 146–154.

1981, *British Journal of Radiology*, 54, 678–679

Case reports

Combined duodenoscopic and transhepatic approach to stenosis of the papilla of Vater

By R. R. Mason, F.R.C.S., M.R.C.P., F.R.C.R. and P. B. Cotton, M.D., F.R.C.P.

Department of Radiology and Gastrointestinal Unit, The Middlesex Hospital, Mortimer Street, London W1N 8AA

(Received December 1980)

Duodenoscopic sphincterotomy is now well established as an alternative to surgical intervention for the management of bile duct obstruction. We describe a patient in whom initial failure of sphincterotomy, due to inability to cannulate a stenosed papilla, was overcome by initial dilatation of the papilla with a balloon catheter passed by the transhepatic route.

CASE REPORT

A 79-year-old man underwent emergency cholecystectomy for empyema of the gall bladder. Operative cholangiography showed stones in the common bile duct; the duct was explored and stones were removed.

Post-operative T-tube cholangiography showed three stones remaining (Fig. 1). Two attempts at duodenoscopic sphincterotomy failed; the papilla was small and firm, and could not be entered. The patient was discharged with the T-tube in place. Five weeks after surgery, the stones were extracted percutaneously via the T-tube track, using the technique now well established in this country (Mason, 1980) and overseas (Burhenne, 1974; Mazzariello, 1976). A 12 FG catheter was left draining the bile duct.

Very little contrast medium had entered the duodenum on any of the cholangiograms, and flow was not significantly improved after stone extraction. The radiological appearances suggested a stricture at the papilla. We were not prepared at that stage to advise any further procedure on the papilla which might yet have been normal; there was no evidence of tumour at duodenoscopy. The drainage tube was closed, with a view to following clinical progress and subsequent tube removal; if a biliary fistula persisted after 24 hours, this would be taken as evidence of significant papillary obstruction, and the T-tube track would be recatheterized. Unfortunately the catheter fell out at home; by the time this was reported five days later, the track had closed and could not be renegotiated. The patient was unwell with intermittent fevers and persistent elevation of the serum alkaline phosphatase. It was felt that a further attempt to improve drainage was urgently indicated.

Under general anaesthesia, a PE 160 catheter was introduced into the bile duct by the percutaneous transhepatic route (Marions and Wiechel, 1974) and advanced into the duodenum. Even with this catheter as a guide, the papilla would not accept the sphincterotomy knife. The PE 160 catheter was changed, over a guide wire, to a 7 FG angioplasty catheter. The balloon was positioned in the papilla, inflated to 9 mm diameter (under endoscopic view) and slowly withdrawn into the bile duct (Fig. 2). It was then simple at duodenoscopy to pass the sphincterotomy knife into the dilated sphincter, and to perform sphincterotomy. Further biopsies were taken from within the sphincterotomy to exclude the possibility of sub-mucosal malignancy. The patient recovered quickly without further fever, and the transhepatic tube was gradually removed over the subsequent 48 hours. The patient was well four months later.

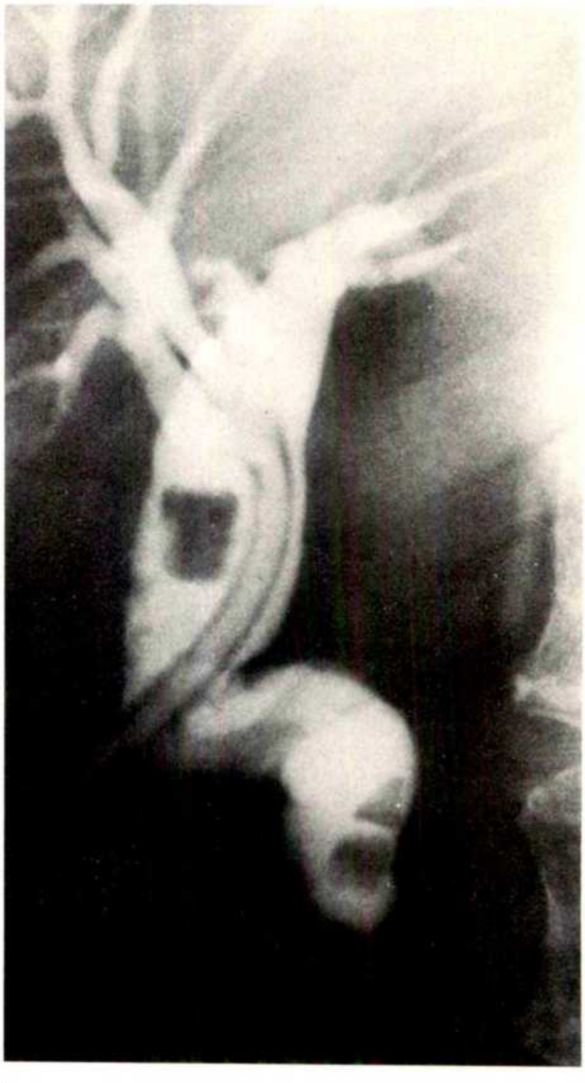


FIG. 1.

Post-operative T-tube cholangiogram showing retained bile duct stones. Contrast medium has not entered the duodenum.

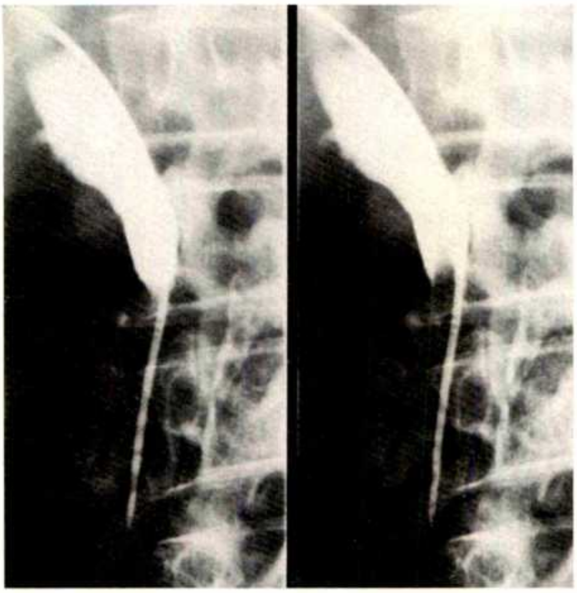


FIG. 2.

Angioplasty catheter placed through ampulla, before and after inflation of balloon.

DISCUSSION

Biliary surgery is accompanied by an appreciable morbidity and mortality in elderly and frail patients (Glenn and Hays, 1955; Vellacott and Powell, 1979). Non-surgical techniques are increasingly being used. The radiological procedures include percutaneous stone extraction through the T-tube track and liver, and percutaneous transhepatic drainage and insertion of endoprostheses for benign (Molnar and Stockum, 1978) and malignant strictures (Dooley *et al.*, 1979). Duodenoscopic sphincterotomy is an effective method for the removal of bile duct stones (Cotton, 1980) and is also being employed in the management of biliary obstruction due to fibrosis or malignancy (Safrany, 1978; Laurence and Cotton, 1980). Failure to achieve bile duct cannulation at duodenoscopy occurs in less than 10% of patients. In such instances the radiological and endoscopic techniques can be combined. In a previously reported case (Mason and Cotton, 1980) endoscopic sphincterotomy was used in conjunction with cholecystostomy catheterization, and in the present case with transhepatic intubation and papillary dilatation.

REFERENCES

BURHENNE, H. J., 1974. The technique of biliary stone extraction. *Radiology*, *113*, 567–572.

COTTON, P. B., 1980. Non-operative removal of bile duct stones by duodenoscopic sphincterotomy. *British Journal of Surgery*, *67*, 1–5.

DOOLEY, J. S., DICK, R., OLNEY, J. and SHERLOCK, S., 1979. Non-surgical treatment of biliary obstruction. *Lancet*, *ii*, 1040–1043.

GLENN, F. and HAYS, D. M., 1955. The age factor in the mortality rate of patients undergoing surgery of the biliary tract. *Surgery, Gynecology and Obstetrics*, *100*, 11–18.

LAURENCE, B. H. and COTTON, P. B., 1980. Decompression of malignant biliary obstruction by duodenoscopic intubation of bile duct. *British Medical Journal*, *i*, 522–523.

MARIONS, D. and WIECHEL, K.-L., 1974. Röntgenologisk ikterusutredning. *Opuscula Medica, Suppl. XXXII.*

MASON, R. R., 1980. Percutaneous extraction of retained gallstones via the T-tube track—British experience of 131 cases. *Clinical Radiology*, *31*, 497–499.

MASON, R. R. and COTTON, P. B., 1980. Combined endoscopic and percutaneous trans-cystic approach to a retained common duct stone. *British Journal of Radiology*, *53*, 38–39.

MAZZARIELLO, R. M., 1976. Residual biliary duct stones; non-operative treatment of 570 patients. *Surgery Annual*, *8* (Appleton-Century-Crofts, New York), 113–144.

MOLNAR, W. and STOCKUM, A. E., 1978. Transhepatic dilatation of choledochoenterostomy strictures. *Radiology*, *129*, 59–64.

SAFRANY, L., 1978. Endoscopic treatment of biliary tract diseases. *Lancet*, *ii*, 983–985.

VELLACOTT, K. D. and POWELL, P. H., 1979. Exploration of the common bile duct, a comparative study. *British Journal of Surgery*, *66*, 389–391.

Biliary sludge—ultrasonic appearance simulating neoplasm

By B. Anastasi, M.D., D.M.R.D., F.R.C.R. and G. R. Sutherland, F.R.C.P., F.R.C.R.

Department of Radiology, Stobhill General Hospital, Glasgow

(*Received March 1981*)

Biliary sludge is the term applied to the material causing layered ultrasonic echoes in the gall bladder. It may be due to thick or inspissated bile, multiple tiny non-shadowing calculi, pigment granules or cholesterol crystal formation, haemobilia, purulent bile or pus (Conrad *et al.*, 1979; Buschi *et al.*, 1979; Filly *et al.*, 1980). The appearance usually has a medium-to-coarse echo pattern, shows a horizontal fluid/fluid interface, no acoustic shadowing and being gravity-dependent moves when the patient assumes an oblique or lateral decubitus position (Anderson and Harned, 1977; Conrad *et al.*, 1979; Filly *et al.*, 1980; Leopold *et al.*, 1976). The appearance of biliary sludge may be variable, however; movement under gravity may be very slow (Filly *et al.*, 1980); in empyema of the gall bladder diffuse echogenic densities may fill the gall bladder and show no gravity dependence or layering effect (Kane, 1980). Inspissation of bile in long-standing biliary obstruction may appear as a uniform solid mass lying in the position of the gall bladder (Weeks *et al.*, 1977).

In this paper we report four cases of biliary sludge with an unusual appearance. The patients were referred with symptoms of gall-bladder disease or obstructive jaundice and in each case the ultrasonic picture suggested the presence of a sessile tumour arising from the gall-bladder wall.

Case Reports

Case 1

A 53-year-old female was hospitalized with a three-day history of pyrexia, vomiting and right upper quadrant pain. A tender globular mass was palpable in the right subcostal region. No opaque calculi or gall-bladder opacification were demonstrated on IV cholangiography, but the common bile duct was slightly dilated with suspicion of a calculus at its distal end. Gall-bladder ultrasonography demonstrated a well-defined heaped mass of medium-to-coarse echoes, with one or two areas of acoustic shadowing (Fig. 1). The possibility of a gall-bladder tumour associated with cholelithiasis was considered. A repeat ultrasound the following day demonstrated the presence of gall-stones but the previously noted mass had disappeared. The patient's condition did not improve. Cholecystectomy was performed revealing a thickened and inflamed gall bladder containing pus and gall stones. The bile duct was also inflamed and contained purulent bile together with calculous debris at its lower end.

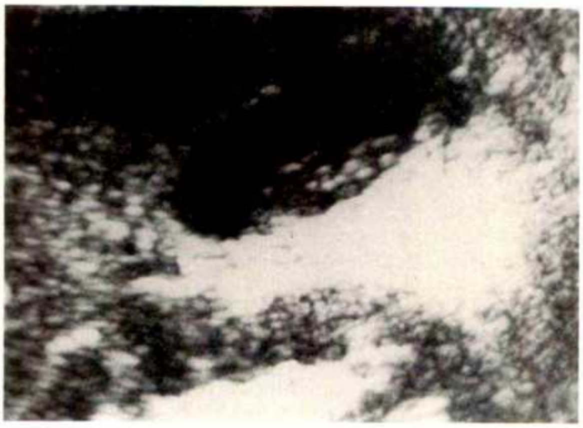


Fig. 1. *Case 1.*

Longitudinal scan, showing well-defined mass lesion with areas of higher intensity reflections. Acoustic shadowing not evident on this section.

Case 2

A 41-year-old male was admitted for investigation of jaundice. Three years previously he was stabbed and a severed common bile duct was repaired. Since then he had suffered from intermittent bouts of cholangitis. On admission biochemical investigation showed bilirubin 90 μmol/l and alk. phos. 1300 i.u./l. Ultrasonography showed dilatation of the intrahepatic biliary radicles, common hepatic duct and the upper part of the common bile duct. The distal part was of normal calibre. Gall-bladder ultrasonography demonstrated a well-defined clump of coarse intraluminal echoes with no acoustic shadowing in keeping with a mural tumour (Fig. 2). Repeat ultrasound two days later showed disappearance of the gall-bladder mass and slight but diffuse irregularity along the dependent gall-bladder wall suspicious of gravel. A stenosed segment of common bile duct was demonstrated by PTC. At surgery the gall bladder was found to be thick-walled, distended and full of thick bile and a quantity of calculous debris.

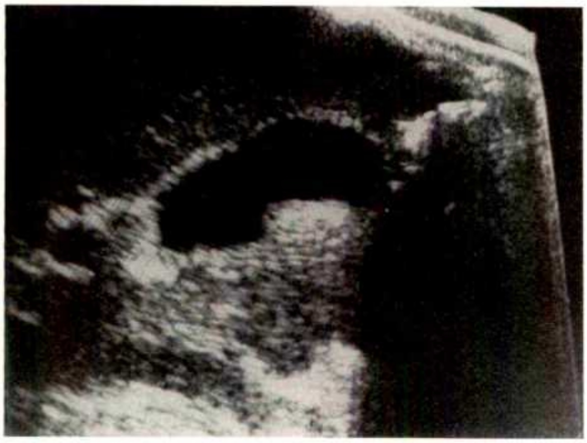


Fig. 2. *Case 2.*

Well-defined mass lesion without acoustic shadowing.

Case 3

An 85-year-old female was hospitalized after a five-week history of vomiting, anorexia, weight loss and abdominal distension. She had an episode of melaena, was slightly jaundiced and her stools were pale and urine dark. Her bilirubin was 61 μmol/l and alk. phos. 173 i.u./l. Clear ascitic fluid was aspirated and there was no evidence of

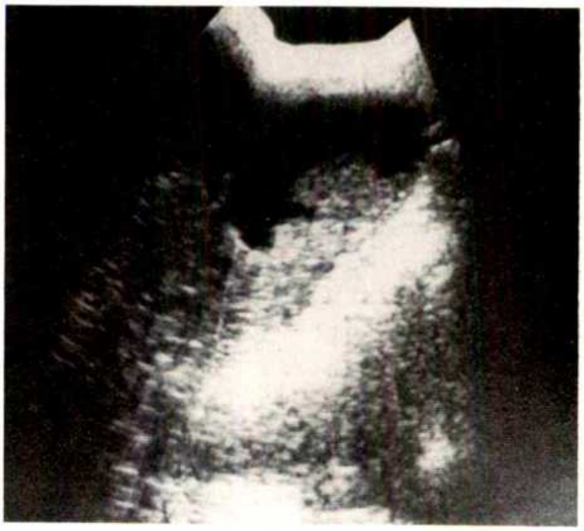


Fig. 3. *Case 3.*

Longitudinal scan. Large polypoidal mass-like lesion without evidence of acoustic shadowing.

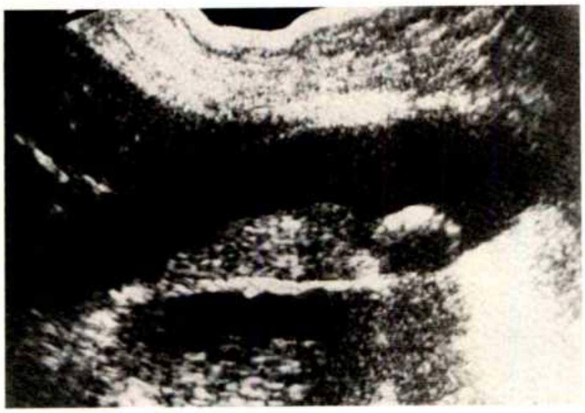


FIG. 4. *Case 4.*

Slightly lobulated mass with homogeneous echoes associated with an adjacent calculus.

malignant cells. On ultrasound examination the intrahepatic and common bile ducts were dilated down to the level of a large poorly demarcated tumour mass in the region of the pancreas. The gall bladder was enlarged, containing a lobulated mass in its dependent portion (Fig. 3). The patient became more jaundiced, her condition deteriorated and she died ten days later. Autopsy showed a complete block of the dilated common bile duct by a pancreatic carcinoma. The gall bladder was distended and contained a large amount of thick mucoid bile which adhered tenaciously to the mucosa.

Case 4

A 73-year-old female was admitted with a three-week history of jaundice associated with pale stools and dark urine and accompanied by nausea, poor appetite and loss of weight. On ultrasound examination the hepatic and common bile ducts were dilated, and the gall bladder was distended, containing a large gall-stone and what appeared to be a slightly lobulated homogeneous soft tissue mass (Fig. 4). At percutaneous cholangiography the lower end of the common bile duct showed a rounded filling defect associated with a rat-tail sign. The surgical findings were that of a papillary adenocarcinoma of the ampulla of Vater obstructing the common bile duct. The distended oedematous gall bladder was found to contain debris and a large gall-stone.

DISCUSSION

In these four cases the ultrasonic picture of biliary sludge was atypical. The dependent portion of the gall bladder contained a homogeneous echogenic mass rather than horizontal layering, the echoes being heaped up or clumped together causing a tumour-like appearance. The margins of the mass were smooth and rounded or lobulated, there was no acoustic shadowing and no evidence of gravity dependence in the oblique or left lateral decubitus position. Because of the unusual appearances, the examination was repeated in two of the patients (Cases 1 and 2) within a few days. In both cases the tumour-like mass had disappeared, while Case 2 showed some echoes dispersed against the dependent wall of the gall bladder. Unfortunately Cases 3 and 4 had no repeat examination as one died and the other was operated on before this could be done. At surgery or autopsy the contents of the four gall bladders were found to be biliary debris, thick inspissated bile or pus, with gall-stones in two of the cases. *In vitro* studies of the gall-bladder contents from Case 4 showed an ultrasonic pattern similar to the *in vivo* examination and that gravity dependence was greatly delayed, the sludge taking over two hours to slide to the lowest portion of the container.

We present these cases as a reminder that biliary sludge has a variable appearance, may not show the signs previously described for its diagnosis and may even look like a solid tumour. We consider that the mass effect is due to temporary clumping of highly viscous material due to bile stasis in the gall bladder. Its altered appearance is almost certainly due to a different physico-chemical state of the bile in the gall bladder at the time of the second examination. When such lesions are discovered the examination must be repeated as this will generally allow the diagnosis to be made.

REFERENCES

ANDERSON, J. C. and HARNED, R. K., 1977. Gray scale ultrasonography of the gall bladder: an evaluation of accuracy and report of additional ultrasound signs. *American Journal of Roentgenology*, *129*, 975–977.

BUSCHI, A. J., BRENBRIDGE, A. N., COCHRANE, J. A. and TEATES, C. D., 1979. A further observation on gall-bladder debris. *Journal of Clinical Ultrasound*, 7, 152–153.

CONRAD, M. R., JANES, J. O. and DIETCHY, J., 1979. Significance of low level echoes within the gall bladder. *American Journal of Roentgenology*, *132*, 967–972.

FILLY, R. A., ALLEN, B., MINTON, M. J., BERNHOFT, R. and WAY, L. W., 1980. *In vitro* investigation of the origin of echoes within biliary sludge. *Journal of Clinical Ultrasound*, *8*, 193–200.

KANE, R. A., 1980. Ultrasonographic diagnosis of gangrenous cholecystitis and empyema of the gall bladder. *Radiology*, *134*, 191–194.

LEOPOLD, G. R., AMBERG, J., GOSINK, B. B. and MITTELSTAEDT, C., 1976. Gray scale ultrasonic cholecystography: a comparison with conventional radiographic techniques. *Radiology*, *121*, 445–448.

WEEKS, L. E., MCCUNE, B. R., MARTIN, J. F. and O'BRIEN, T. F., 1977. Unusual echographic appearance of a Courvoisier gall bladder. *Journal of Clinical Ultrasound*, *5*, 341–342.

1981, *British Journal of Radiology*, *54*, 682–683

Case reports

An unusual case of subcutaneous emphysema

By S. A. Thompson, M.B., B.S., J. S. Harper, M.B., B.S., F.R.C.R. and P. Millican, M.B., B.S., F.R.C.S., F.R.A.C.S.

Princess Alexandra Hospital, Brisbane, Queensland, Australia

(Received November 1980 and in revised form February 1981)

Subcutaneous emphysema of gastro-intestinal origin is a rare occurrence, particularly when localized in the lower limb (Fox *et al.*, 1978; Oetting *et al.*, 1955). Until recently 51 cases of subcutaneous emphysema of gastro-intestinal origin have been reported and 23 of these were confined to the lower limb. To our knowledge the aetiology of this patient's soft tissue gas is unique.

CASE REPORT

A 51-year-old male was admitted to our hospital on 3/10/79 complaining of left hip pain of five months' duration which had become more severe over the preceding three weeks. He was unable to weight bear for this period and for two days there had been swelling in the hip region.

On examination, temperature was 37.9°C, pulse 88 per minute. Abdominal examination revealed mild tenderness deep in the left iliac fossa but there were no other abdominal signs or symptoms. On rectal examination, there was mild benign prostatic hypertrophy and tenderness and fullness of the left pararectal space. There was pain on movement of the left hip and swelling of the thigh. Hb. was 10.7 mg%, WBC 12600, glucose, urea and electrolytes within normal limits. Past history included asthma, for which the patient took Prednisone 5 mg t.d.s. and Ventolin via inhaler, appendicectomy and tonsillectomy. In 1967 the patient had sustained a displaced fracture of the left acetabulum which was reduced openly with two Stuck nails (made of vitallium-cobalt alloy). Pelvic X ray revealed two nails in an acetabular fracture, one of which projected 2–3 cm into the true pelvis. There was gas over the upper femur between the soft tissue planes of the left hip and thigh. The fluctuant area over the scar on the left thigh was drained with syringe and 10 ml of dark brown pus obtained which grew staphylococci, streptococci, bacteroides and gram negative bacilli.

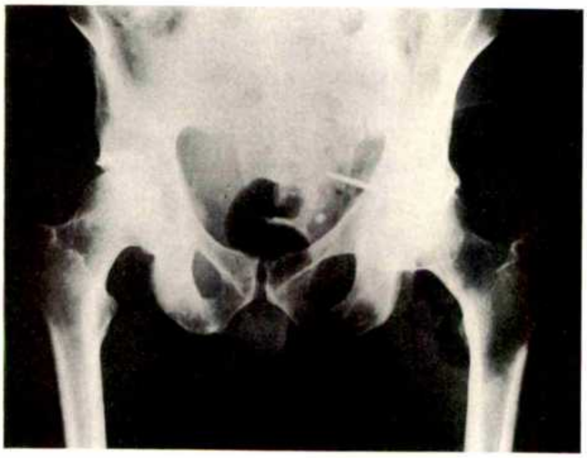


FIG. 1.

Pelvic X ray showing subcutaneous emphysema of left hip and two Stuck nails in left acetabulum.

Definitive treatment undertaken the following day was drainage of the abscess cavity under GA which resulted in vast symptomatic improvement. The patient returned to theatre on 5/10/79 to divert the faecal fistula: one of the pins had perforated the distal sigmoid forming a tight fistulous track via the sciatic foramen to the thigh. There was no spillage of faeces into the abdomen. The sigmoid perforation was oversewn and a drain inserted.

Post-operative course was marred by right middle lobe collapse/consolidation which improved with physiotherapy. Transfusion for low haemoglobin and catheterization for two episodes of urinary retention were also required. By the time of discharge the patient was fully mobilized.

DISCUSSION

Subcutaneous emphysema of the lower limb is a rare condition and of 23 cases so far reported 65% have died (Fox *et al.*, 1978; Nicell *et al.*, 1975). Although a significant number occurred in the pre-antibiotic era, this mortality rate does indicate that it is a serious condition and early diagnosis is vital if mortality and morbidity are to be reduced. Perplexing initial presentation results in delayed initiation of definitive therapy.

The commonest causes of subcutaneous emphysema are (Starer, 1975):

(1) break in continuity of respiratory tract;
(2) gas-forming infection;
(3) Atmospheric air via break in skin;
(4) Rent in the gastro-intestinal tract (Oetting *et al.*, 1955).

The two main pathways for the passage of gas from gastro-intestinal tract to thigh are via the inguinal canal anteriorly or the sciatic foramen posteriorly (Fox *et al.*, 1978). In this case, the latter occurred and the patient had five months of pain suggesting that the nail in his acetabulum had perforated the bowel for at least that period. However, it is difficult to know whether the nail had slipped from its original position, since he had his surgery in another city 13 years before and no early post-operative films were available to us.

The commonest causes of lower limb subcutaneous emphysema of gastro-intestinal origin are ruptured diverticulum of sigmoid, appendicitis and cancer of left colon (Robbins *et al.*, 1977). An overall finding is that gas confined to the leg usually has its origin in the lower intestine.

Patients usually present diagnostic problems and correct diagnosis has often not been made until surgical exploration or autopsy. They rarely exhibit signs of peritonism and hip pain is the most common complaint. Once crepitant cellulitis has developed a rapid downhill path often ensues and plain X rays should be used early to demonstrate gas in the soft tissues between muscles along fascial planes, distinguishing this condition from gas gangrene where gas is found within the muscles (Ainsworth, 1959).

Stuck nails are in our experience rarely used to treat acetabular fracture, screws being more commonly employed. Internal displacement of a pin is generally an uncommon sequela of this type of fracture but the use of a nail rather than a screw may have increased the chance of this occurrence.

REFERENCES

AINSWORTH, J., 1959. Emphysema of leg following perforation of pelvic colon or rectum. *British Journal of Radiology*, *32*, 54.

FOX, T., GOMEZ, J. and BRAVO, J., 1978 Subcutaneous emphysema of lower extremity of gastro-intestinal origin. *Diseases of Colon and Rectum*, *21*, 357–360.

NICELL, P., TABRISHY, J., LINSTROM, R. and PETER, M., 1975. Thigh emphysema and hip pain secondary to gastro-intestinal perforation. *Surgery*, *78*, 555–559.

OETTING, H., KRAMER, N. and BRANCH, W., 1955. Subcutaneous emphysema of gastro-intestinal origin. *American Journal of Medicine*, *19*, 872–885.

ROBBINS, P., SUTHERLAND, E., NGJARIAN, J. and BERNSTEIN, W., 1977. Emphysema of leg as presenting sign of large intestine perforation. *Diseases of Colon and Rectum*, 144–148.

STARER, F., 1975. The soft tissues. In *Text Book of Radiology*. 2nd edit. Ed. by D. Sutton, (Churchill Livingstone, Edinburgh) p. 1090.

Giant diverticulum arising from the transverse colon of a patient with diverticulosis

By K. J. Wallers, M.B., Ch.B., D.M.R.D.

Department of Radiology, Southern General Hospital, Glasgow

(*Received February 1981*)

Acquired giant diverticulum is an uncommon but well-recognized finding in patients with diverticular disease of the colon. Fifty-one cases have been reported so far in the English language literature (Kricun *et al.*, 1980). In forty-eight cases the diverticulum arose from the sigmoid colon; in two from descending colon (Ferguson and Boinis, 1966; Kricun *et al.*, 1980); but in only one case from the transverse colon (Sagar, 1973).

A further case of a solitary giant diverticulum arising from the transverse colon of a patient with extensive diverticulosis is reported. Because of its situation high in the abdomen on plain radiographs the diverticulum was initially mistaken for a lesion arising from the upper gastrointestinal tract. Barium follow-through examination provided the correct diagnosis.

CASE REPORT

A previously well 66-year-old male presented with a four-day history of constipation, upper abdominal pain and slight abdominal distension.

On examination there was diffuse upper abdominal tenderness and a vague mass could be felt in the epigastrium. He had no fever and white blood cell count was normal. He denied any previous episodes of a similar nature, or indeed any previous gastrointestinal symptoms.

Radiological findings

Plain films of the abdomen demonstrated a large (15 cm diameter) oval gas shadow in the upper abdomen a little to the left of the mid-line containing a gas-liquid level (Fig. 1). A small amount of gas was present in the gastric fundus separate from, but partially overlapping, the gas shadow. The transverse colon loaded with faeces was visible running just below the shadow.

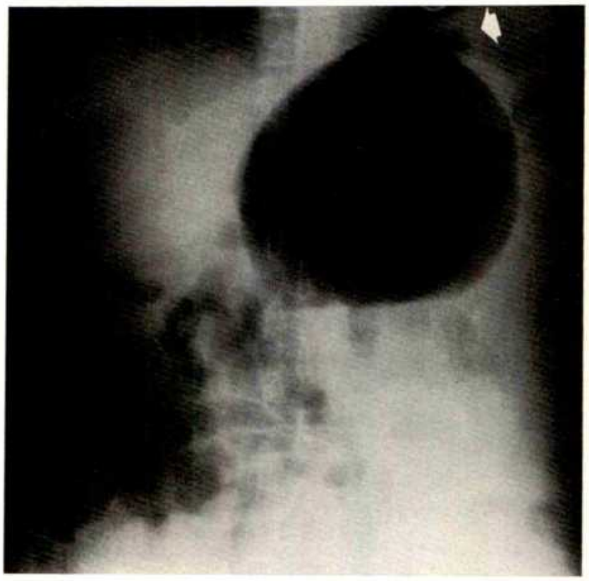


FIG. 1.

Erect film of the abdomen showing the gas shadow in the left upper quadrant of the abdomen with a gas-liquid level. The arrow points to air in the gastric fundus.

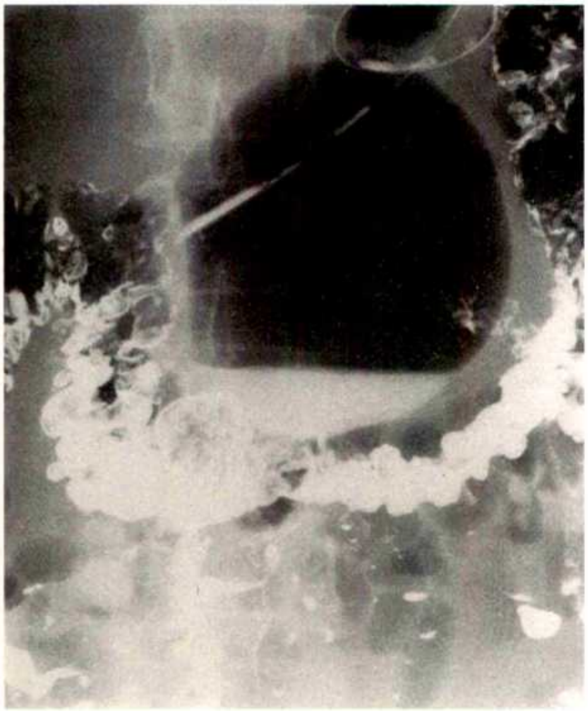


FIG. 2.

Late film from the barium follow-through. There are multiple small colonic diverticula. The intimate relationship of the giant diverticulum to transverse colon is shown as is the increased density of the liquid within the diverticulum, indicating entry of barium from the bowel. (Naso-gastric tube lies coiled in the stomach).

Barium meal showed no abnormality in, or apparent connection of the gas shadow with, the upper gastrointestinal tract. Delayed PA and lateral films of the abdomen with the patient erect taken two hours after the meal showed the gas shadow lying separate from, and antero-inferiorly in relation to, the stomach but just above the transverse colon and immediately beneath the anterior abdominal wall.

Further examination six hours after the meal confirmed the intimate relationship of the gas shadow to the transverse colon and showed a definite increase in density of the fluid within the cavity, confirming connection with the bowel lumen (Fig. 2). Extensive diverticulosis was present in transverse and descending colon.

Surgical and pathological findings

Laparotomy confirmed the presence of a large thin-walled diverticulum arising from the mesenteric border of the transverse colon, with which it communicated by a 1 cm wide neck. The diverticulum was excised at its neck. Post-operative recovery was uneventful.

Histological examination of the diverticulum revealed a thin fibrous tissue wall with a lining of granulation tissue. There was no evidence of smooth muscle or nervous tissue in the wall.

DISCUSSION

The aetiology of giant colonic diverticula (GCD) remains unclear. A few, mainly those occurring in younger patients, are probably true congenital diverticula or communicating reduplication cysts and can be differentiated histologically by the presence of all layers of bowel in their wall. The majority however occur in older patients with diverticular disease and appear to represent pseudodiverticula which have undergone massive gaseous distension.

On plain abdominal radiographs GCD appear as large, smoothly marginated, round or oval gas shadows, usually in the lower or mid abdomen. Size is variable and roughly 25% contain a gas-liquid level. Rarely they are multiple. Once suspected, confirmation is best provided by barium enema which will demonstrate the intimate relationship of the GCD to colon. Filling of the diverticulum with barium confirms connection with the bowel lumen and occurs in about 60% of cases (Kricun *et al.*, 1980).

Complications occur in about 12% of cases, more frequently in recent series (three out of five cases—Kricun *et al.*, 1980). Complications reported include volvulus (one case), subserosal perforation with or without abscess formation (three cases), perforation with pneumoperitoneum (one case) and adenocarcinoma within the diverticulum (one case).

Elective excision of the diverticulum is thus the treatment of choice.

REFERENCES

FERGUSON, W. H. and BOINIS, G. A., 1966. A giant diverticulum of the colon: report of a case. *Medical Annual of the District of Columbia*, *35*, 66–68.

KRICUN, R., STASIK, J. J., REITHER, R. D. and DEX, W. J., 1980. Giant colonic diverticulum. *American Journal of Roentgenology*, *135*, 507–512.

SAGAR, S., 1973. Giant solitary diverticulum of the transverse colon with diverticulosis. *British Journal of Clinical Practice*, *27*, 145–146.

1981, *British Journal of Radiology*, 54, 685–686

Case reports

Pseudo tumours of the colon due to adhesions

By Z. F. Boulis, F.R.C.S., F.R.C.S.(Ed.), D.M.R.D. and D. R. Osborne, F.R.C.S.

Royal Free Hospital, London NW3

(*Received September 1980 and in revised form January 1981*)

Large bowel pseudo tumours caused by adhesions and bands are rare but cause a diagnostic problem as they can mimic more serious disease. The lesions characteristically occur in the transverse and the sigmoid colon, the most important underlying cause being previous surgery. Pre-operatively the diagnosis cannot be made with certainty and if a pseudo tumour is considered, colonoscopy is recommended and may help avoid laparotomy. If the diagnosis is suspected because of negative findings at laparotomy, peroperative colonoscopy can avoid resection.

CASE REPORT

A 60-year-old housewife had a recent onset of paraumbilical pain, constipation and rectal bleeding. She had undergone appendicectomy and Caesarian section 40 and 30 years ago respectively. Physical examination suggested a mass in the left iliac fossa, rectal examination being normal. Sigmoidoscopy revealed traces of blood in the upper rectum and carcinoma or diverticular disease of the colon were considered in the differential diagnosis. Barium enema showed one segment of deformity with mucosal irregularity in the distal transverse colon, and another segment of narrowing in the sigmoid colon (Figs. 1 and 2). The sigmoid lesion showed thumb-printing of the lateral wall suggestive of local ischaemia (Fig. 3). Such areas did not alter with 0.5 mg glucagon IV and the appearance of the transverse colonic lesion suggested a carcinoma. At laparotomy there were several adhesions involving the transverse, descending and sigmoid colons. The adhesions were dissected clear and on palpation the colon was normal apart from slight thickening at the sites in question. There was no sign of malignancy. In view of the barium enema findings, peroperative colonoscopy was performed. This allowed close examination of the transilluminated bowel wall and showed the mucosa of the relevant sites to be normal apart from oedema. Biopsies were taken and the abdomen closed, recovery being uneventful. Histology showed a mild inflammatory reaction, with some necrotic debris and granulation tissue.

DISCUSSION

Weibel and Manjo (1973) estimate that up to 68% of patients undergoing abdominal surgery develop adhesions. Such adhesions can result in radiological changes on a barium enema resembling a variety of lesions, including neoplasm, haematoma, endometriosis and lymphatic cyst (Kyaw and Koehler, 1972). The changes are essentially the result of fibrous connective tissue replacing the appendices epiploicae as a result of inflammatory change. The inflammation may result from previous surgery, torsion, infection or vascular occlusion. The appendices

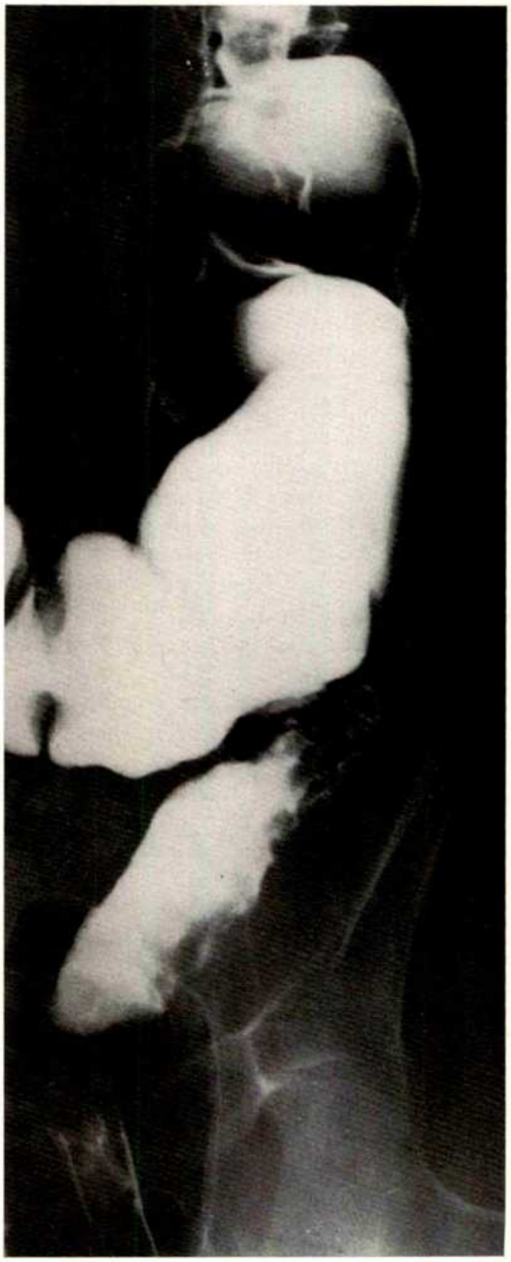


FIG. 1.

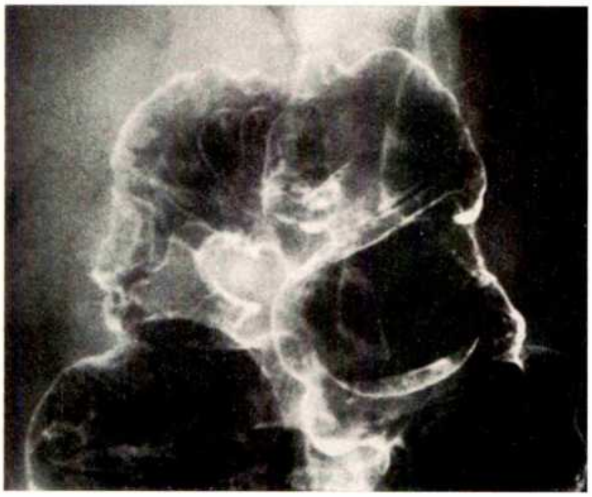


FIG. 2.

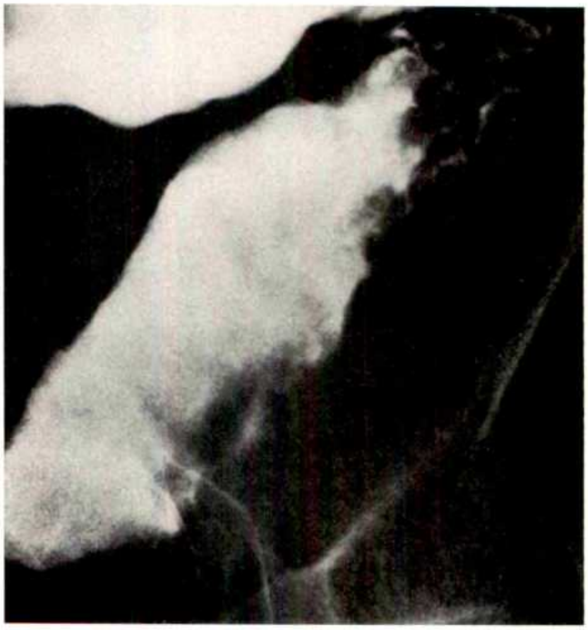


FIG. 3.

epiploicae, though found over the entire colon, are most abundant in the transverse and sigmoid colon. The ultimate result of their inflammation is adherence of the bowel wall by fibrous connective tissue to adjacent loops of bowel or nearby organ (Kirsh and Drosd, 1959).

The clinical symptoms are non-specific and include changes in bowel habit and rectal bleeding giving a wide differential diagnosis. Kyaw and Koehler (1972) suggest the following features are useful in the diagnosis of pseudo tumour due to adhesions:

(1) history of previous surgery or inflammatory disease of the abdomen or pelvis;

(2) intact mucosa at the site of abnormality. This was not a radiological feature in the case under review;

(3) evidence of involvement of adjacent small bowel loops. Bartram (1980) has shown the importance of the small bowel enema in this respect;

(4) location of the lesion in the transverse or sigmoid colon.

In the present patient, the appearance seen in the mucosa at colonoscopy may have represented localized ischaemic changes secondary to the adhesions. The rectal bleeding may be explained by the ischaemic colitis. It is noted that the pelvic colon shows "thumb-printing" of one wall only (Fig. 3). This is contrary to the conventional thumb-printing of both walls due to main vessel occlusion and to our knowledge has not been described before; it could be explained by the concept of localized ischaemia from adhesions. The fact that it is on the anti-mesenteric border, being less vascular, further supports such a concept.

Once the diagnosis is considered, pre-operative colonoscopy is imperative. A primary carcinoma being essentially a mucosal lesion, can be excluded by an experienced colonoscopist. If colonoscopy is negative and adhesions thought to be responsible, a laparotomy can be avoided unless obstructive symptoms develop.

ACKNOWLEDGMENTS

We wish to thank Dr. R. Dick, Consultant-in-charge, Department of Radiology, for giving advice and reading the text, Professor K. Hobbs, Professor of Surgery, under whose care the patient was, and M. O'Daye for her secretarial work.

REFERENCES

BARTRAM, C. I., 1980. The radiological demonstration of adhesions following surgery for inflammatory bowel disease. *British Journal of Radiology*, *53*, 650–653.

KIRSH, D. and DROSD, R. E., 1959. Roentgen change in disease of the appendices epiploicae. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *81* 640–649.

KYAW, M. M. and KOEHLER, P. R., 1972. Pseudotumours of colon due to adhesions. *Radiology*, *103*, 597–599.

WEIBEL, M. A. and MANJO, G., 1973. Peritoneal adhesions and their relationship to abdominal surgery. *American Journal of Surgery*, *126*, 345–353.

1981, *British Journal of Radiology*, *54*, 687–688 AUGUST 1981

Case reports

Pre-natal ultrasound demonstration of lymphangiectasia in the mesentery of the small bowel

By K. C. Dewbury, B.Sc., M.B., F.R.C.R., K. S. Rao, M.B., B.S., F.R.C.S. and V. Poll, Ph.D.

Department of Radiology, Southampton General Hospital, Southampton SO9 4XY

(*Received November 1980 and in revised form February 1981*)

The finding of cystic abnormalities in the fetal abdomen is being increasingly reported. Double cystic structures in the fetal abdomen are typically seen in duodenal atresia (Gee and Abdullah, 1978). A similar appearance may be produced by bilateral hydronephrosis (Hately and Nicholls, 1979). Similar appearances have also been reported in a case of a choledochal cyst (Dewbury *et al.*, 1980).

We report a case where multiple small cysts, which later proved to be lymphangiectasia in the mesentery of the small bowel, were seen filling the fetal abdomen. This is an extremely rare condition, and, to our knowledge, no similar case has been previously reported in the literature of either surgical pathology or diagnostic radiology.

CASE REPORT

A 23-year-old primigravida at 33 weeks' gestation was referred for ultrasound examination with a history of slight vaginal bleeding. The examination showed a single live fetus consistent in size with dates. A right antero-lateral placenta was shown in the upper segment. In addition, it was noted that the fetal abdomen was filled with small cystic spaces (Fig. 1). The vaginal bleeding subsided with conservative management, and the pregnancy proceeded normally. A second ultrasound examination at 36 weeks again showed the same abnormality of the fetal abdomen. Normal fetal kidneys were identified, and the bladder was full at the time of this examination. A renal anomaly was therefore considered unlikely. The most likely diagnosis at this stage was considered to be a bowel atresia, although the stomach itself did not appear to be unduly distended.

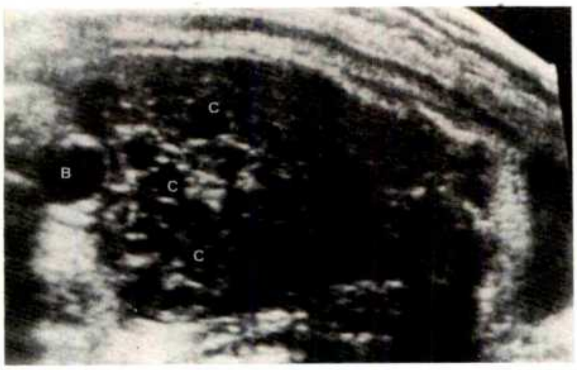


FIG. 1.

A longitudinal scan through the fetal abdomen at 33 weeks of gestation, showing multiple small cystic spaces (C). B, bladder.

Labour was induced at 39 weeks, which resulted in a normal vaginal delivery of a live male infant weighing 3950 g with an Apgar score at one minute of 9. Initial clinical examination of the baby showed abdominal distension, but no discrete masses were palpable. The baby was otherwise well, fed normally and passed normal-coloured stools. An intravenous urogram on the second day of life showed normal kidneys. An ultrasound examination was performed on the third day after birth, which showed the abdomen to be full of a complex cystic mass. A number of the cysts contained fine low-level echoes (Figs. 2A, B). The presence of

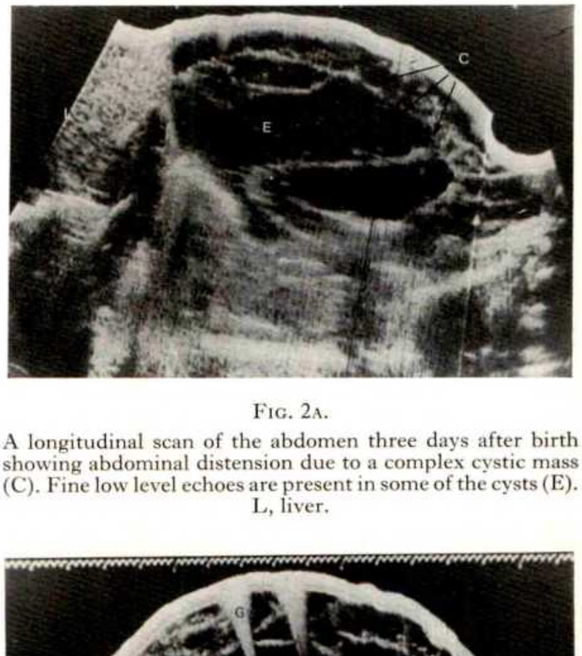


FIG. 2A.

A longitudinal scan of the abdomen three days after birth showing abdominal distension due to a complex cystic mass (C). Fine low level echoes are present in some of the cysts (E). L, liver.

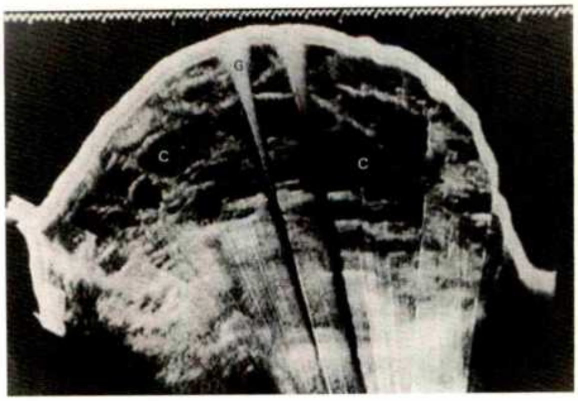


FIG. 2B.

A transverse scan at the same time as Fig. 2A at the level of the umbilicus. C, cysts; G, gas-containing bowel.

Address for reprints: Dr. K. C. Dewbury, Ultrasound Department, Southampton General Hospital, Shirley, Southampton SO9 4XY.

low-level echoes within some of the cysts was thought to represent the presence of mucinous material and an extensive intestinal duplication was considered to be the most likely diagnosis. A bowel atresia was excluded, both by the clinical status and the normal bowel function. A pertechnetate imaging examination showed no ectopic gastric mucosa in the abdomen. Starting on the third day, the baby became increasingly jaundiced with a drop in haemoglobin requiring exchange transfusion. There was one episode of melaena, but there were no signs suggestive of necrotizing enterocolitis on a repeat abdominal radiograph. During this time there was gradual increase in the soft tissue distension of the abdomen.

A laparotomy was carried out on the seventh day of life. At operation, the whole small bowel appeared to have large cysts hanging on either side of the bowel near the mesenteric border. Accidental rupture of one of these cysts resulted in expulsion of a large amount of sequestrated blood, following which the entire cyst was decompressed. There were also several small cysts in the transverse colon, which seemed to have fatty tissue and lymph in them. No bleeding was seen into these cysts. These were biopsied. None of the cysts appeared to communicate with the lumen of the bowel.

Post-operative progress was uneventful, and the serum bilirubin, which peaked at 340 millimoles, rapidly returned to normal levels. Histology showed dilated channels characteristic of a lymphangiectasia within adipose connective tissue. One specimen showed deposits of calcium with associated haemosiderin and non-specific subacute inflammatory cells, almost certainly a haematoma.

Five days post-operatively, a repeat ultrasound examination showed that the abdominal cysts were smaller, although still clearly visible (Fig. 3). At this time there was no longer evidence of low-level echoes within any of the cysts. Since this time the baby has been followed up carefully, as there was always a risk of further haemorrhage into the cysts. The child is now five months old, and repeat scans have been performed at monthly intervals showing no significant change in the appearance of the cysts within the abdomen. The child has continued to thrive, but has recently developed a moderate amount of ascites and small bilateral hydroceles. We speculate that this is secondary to rupture of one of the cysts into the abdominal cavity.

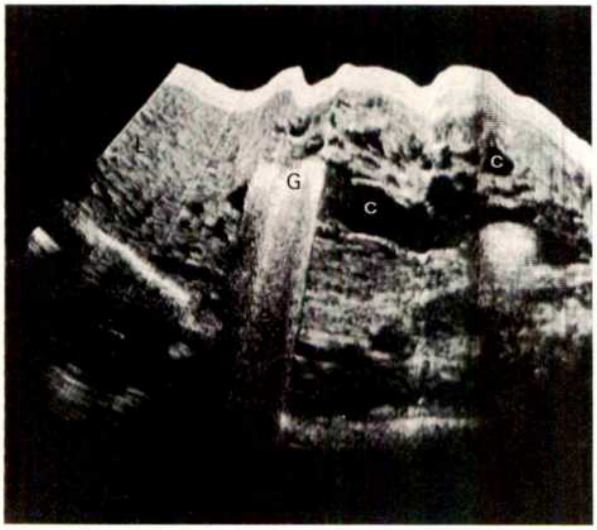


FIG. 3.

A longitudinal scan done on the 12th day of life (five days post-operatively). The cysts (C) now appear smaller. L, liver; G, gas-containing bowel.

DISCUSSION

Primary intestinal lymphangiectasia is described as congenital hypoplasia of the mesenteric lymphatics, resulting in dilated small bowel lymph vessels and an exudative enteropathy. The hypoplasia may occur at a number of sites in the bowel wall, including the lamina propria, submucosa, serosa and mesentery. The clinical manifestations vary widely and often include lymphatic anomalies outside the gastro-intestinal tract (Pomerantz and Waldman, 1963). It may be first diagnosed from the secondary manifestations of an exudative enteropathy (Nugent *et al.*, 1964). All the cases reported in the literature have shown the hallmark lesions of dilatation and lymphangiectasia of the lymphatic vessels of the submucosa and serosa (Waldman, 1966). Most often the histological confirmation has been obtained by per oral jejunal mucosal biopsy.

The case reported by us has not shown any recorded clinical manifestations, and was diagnosed only by the undue abdominal distension and by the ultrasound finding of abdominal cysts. The presence of these large cysts appears to be a unique feature.

REFERENCES

DEWBURY, K. C., ALUWIHARE, A. P. R., BIRCH, S. J. and FREEMAN, N. V., 1980. Antenatal ultrasound demonstration of a choledochal cyst, *British Journal of Radiology*, *53*, 906–907.

GEE, H. and ABDULLAH, U., 1978. Antenatal diagnosis of fetal duodenal atresia by ultrasound scan. *British Medical Journal*, *ii*, 1265.

HATELY, W. and NICHOLLS, B., 1979. The ultrasonic diagnosis of bilateral hydronephrosis in twins during pregnancy. *British Journal of Radiology*, *52*, 989–990.

NUGENT, W., ROSS, J. R. and HURXTHAL, L. M., 1964. Intestinal lymphangiectasia. *Gastroenterology*, *47*, 536–539.

POMERANTZ, M. and WALDMANN, T. A., 1963. Systemic lymphatic abnormalities associated with gastro-intestinal protein loss secondary to intestinal lymphangiectasia. *Gastroenterology*, *45*, 703–711.

WALDMAN, T. A., 1966. Protein losing enteropathy. *Gastroenterology*, *50*, 422–443.

1981, *British Journal of Radiology*, *54*, 689–690

AUGUST 1981

Case reports

The diagnosis by computerized tomography of a parathyroid adenoma presenting as acute pancreatitis

By *N. R. McLean, B.Sc., F.R.C.S.,
Department of Surgery, Stobhill General Hospital, Glasgow G21 3EW
N. C. McMillan, M.B., Ch.B., D.M.R.D. and J. G. Duncan, M.B., F.R.C.S., F.R.C.R.
Department of Radiology, Glasgow Royal Infirmary, Glasgow G4 0SF

(*Received December 1980*)

Factors implicated in the aetiology of acute pancreatitis include biliary tract disease, alcohol abuse and abdominal trauma (Imrie and Whyte, 1975).

Reported is a case of hyperparathyroidism due to a solitary parathyroid adenoma, diagnosed by computerized tomography (CT) but which presented as acute pancreatitis.

CASE REPORT

A previously healthy 20-year-old male was admitted with a 24-hour history of severe constant central abdominal pain and vomiting. There was no history of biliary disease, alcohol abuse or abdominal trauma. On examination he was flushed and toxic with a tachycardia of 114 per minute. He was extremely tender with guarding in the epigastrium and right hypochondrium; bowel sounds were normal.

Plain radiographs of the abdomen were normal, haemoglobin was 16.2 g% and total WBC was 17700. Serum amylase was grossly elevated (4500 i.u./l), albumin was low (34 g/l), calcium markedly raised at 3.45 m.mol/l (corrected to 3.65 m.mol/l for albumin), and phosphate correspondingly reduced at 0.69 m.mol/l. A diagnosis of acute pancreatitis associated with hypercalcaemia was made and he was treated conservatively.

On further questioning he gave a recent history of headaches, dyspepsia and increase in overnight urine volumes. A radiograph of both hands was normal and an ECG showed a shortened QT interval. A mineral metabolism screen revealed a raised serum total and ionized calcium with a normal urinary calcium/creatinine ratio. Serum phosphate was low and there was a reduction in the renal tubular

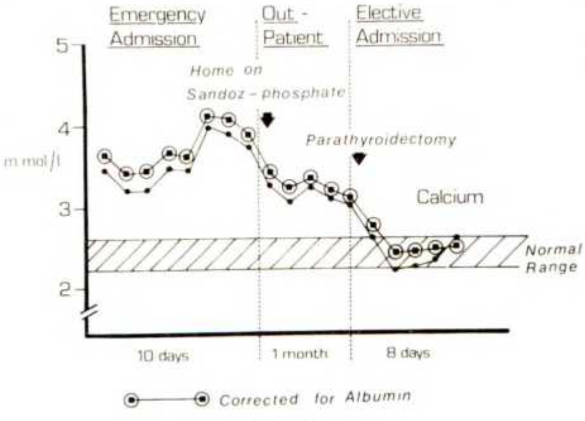


FIG. 1.
Calcium levels.

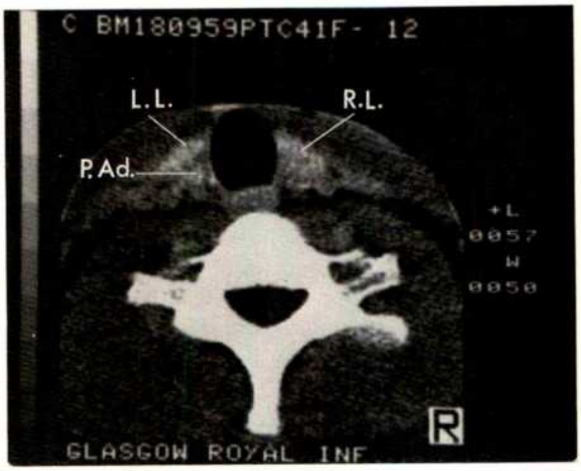


FIG. 2.
CT scan. L.L., Left lobe of thyroid; R.L., Right lobe of thyroid; P.Ad., Parathyroid adenoma.

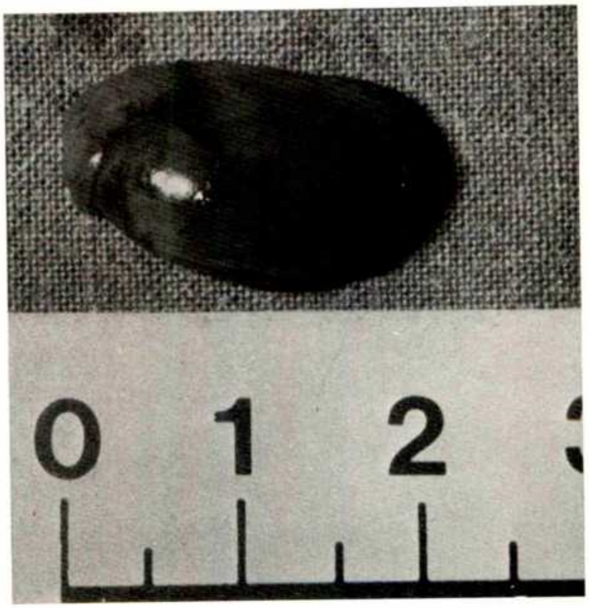


FIG. 3.
Excised parathyroid gland (scale in cm).

---

*Present address: Department of Plastic Surgery, Bangour General Hospital, West Lothian.

absorption of phosphate. The alkaline phosphatase was marginally elevated (123 i.u./l) and the serum parathormone level was raised at 720 ng/l (normal range 0–600 ng/l). Daily calcium levels were measured and these are shown in Fig. 1. He was commenced on sandozphosphate. A CT scan of neck one week later revealed a 2 × 1 cm nodule related to the postero-inferior aspect of the left lobe of the thyroid gland, suggestive of a parathyroid adenoma (Fig. 2).

At operation an enlarged left inferior parathyroid gland was found as reported on CT and excised (Fig. 3). Histological examination confirmed the diagnosis of parathyroid adenoma. Post-operatively his serum calcium fell to normal (Fig. 1) and has remained so for over a year.

DISCUSSION

Although the incidence of acute pancreatitis in hyperparathyroidism is said to be 7% (Wells, 1977), in four recent studies totalling over 600 patients only one case of acute pancreatitis secondary to hyperparathyroidism has been reported (Imrie and Whyte, 1975; Imrie, 1974; Imrie *et al.*, 1978; Ong *et al.*, 1979).

Methods of localizing parathyroid adenomas include neck vein sampling, isotope scanning, ultrasonography, and more recently CT.

Selective venous sampling and radio-immunoassay of parathyroid hormone is an effective method of localization (Bilezikian *et al.*, 1973), selective thyroid vein sampling yielding an accuracy varying between 72% and 82%. In contrast, large vein sampling was shown to be much less helpful with an accuracy of only 29%. This technique is not widely available, is costly, and, being invasive, not without risk.

Traditional isotope scanning using ^{75}Se selenomethionine proved to be unsatisfactory in localizing fuctioning adenomas of the parathyroid glands. A computer-assisted double-isotope technique was shown to be more reliable although the accuracy of localization was still less than 50% (Ell *et al.*, 1975).

A recent report (Edis and Evans, 1979) has claimed a 100% accuracy of localization of parathyroid tumours in ten patients specially selected from several hundred with hyperparathyroidism seen at the Mayo Clinic. A prototype high resolution real-time ultrasound instrument was used and is not yet generally available. Conventional ultrasound techniques have been much less helpful, with wide variations in the accuracy of localization, particularly with smaller tumours (Egdahl, 1979).

CT localization has recently been used as an alternative method (Shimshank *et al.*, 1979) although its reliability in discriminating between thyroid and parathyroid tissue in the neck is variable. In this patient, however, CT was a quick and non-invasive method of localizing a parathyroid adenoma, leading to curative surgery.

ACKNOWLEDGMENTS

We would like to thank Mr. J. A. Garrett for permission to publish details of this case; the photography department of Stobhill General Hospital; and Mrs. C. Haswell for typing the manuscript.

REFERENCES

BILEZIKIAN, J. P., DOPPMAN, J. L., SHIMKIN, P. M., POWELL, D., WELLS, S. A., HEATH, D. A., KETCHAM, A. S., MOUCHIK, J., MALLETTE, L. E., POTTS, J. T. JR. and AURBACH, G. D., 1973. Pre-operative localisation of abnormal parathyroid tissue. *American Journal of Medicine, 55*, 505–513.

EDIS, A. J. and EVANS, T. C. JR., 1979. High-resolution, real-time ultrasonography in the pre-operative location of parathyroid tumours. *New England Journal of Medicine, 301*, 530–534.

EGDAHL, R. H., 1979. Pre-operative parathyroid localisation. *New England Journal of Medicine, 301*, 548–549.

ELL, P. J., TODD-POKROPEK, A. and BRITTON, K. E., 1975. Localisation of parathyroid adenomas by computer assisted parathyroid scanning. *British Journal of Surgery, 62*, 553–555.

IMRIE, C. W., 1974. Observations on acute pancreatitis. *British Journal of Surgery, 61*, 539–544.

IMRIE, C. W., BEASTALL, G. H., ALLAM, B. F., O'NEILL, J., BENJAMIN, I. S. and MCKAY, A. J., 1978. Parathyroid hormone and calcium homeostasis in acute pancreatitis. *British Journal of Surgery, 65*, 717–720.

IMRIE, C. W. and WHYTE, A. S., 1975. A prospective study of acute pancreatitis. *British Journal of Surgery, 62*, 490–494.

ONG, G. B., LAM, K. H., LAM, S. K., LIM, T. K. and WONG, J., 1979. Acute pancreatitis in Hong Kong. *British Journal of Surgery, 66*, 398–403.

SHIMSHANK, R. R., SCHOENROCK, G. J., TAEKMAN, H. P., CIANI, P. and CHAMBERS, R. F., 1979. Pre-operative localisation of a parathyroid adenoma using Computerised Tomography and thyroid scanning. *Journal of Computer Assisted Tomography, 3*, 117–119.

WELLS, S. A., JR., 1977. The parathyroid glands. In *Textbook of Surgery*, 11th ed. (Saunders, Philadelphia) pp. 725–738.

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

The "ten-day rule"

THE EDITOR—SIR,

The "ten-day rule" is a rule of practice intended to reduce the likelihood of irradiation of a pregnancy and is one of the recommendations included in the "Code of Practice for the Protection of Persons against Ionizing Radiations arising from Medical and Dental Use" (1972). The Code recommends that examinations of the lower abdomen should, if practicable, be carried out within ten days following the first day of the menstrual period.

In a recent case of litigation a patient successfully sued an Area Health Authority for damages when her pregnancy was terminated following the realization that she was pregnant at the time of an X-ray examination of the pelvis and lumbar spine. The patient had visited the Casualty Department of the Hospital complaining of pain in the lower back. The Casualty Officer had referred the woman for X-ray examination but had not completed that section of the X-ray request card pertaining to the "ten-day rule".

In the legal action that followed the County Court Judge took the view that, irrespective of both the degree of risk of fetal damage and of the advice of the Consultant Gynaecologist who terminated the pregnancy, the Casualty Officer was liable since he had not demonstrated that he had applied his mind to the possibility of an early pregnancy.

This highlights the necessity for the requesting Clinician to consider the possibility of an early pregnancy and to complete that section of the X-ray request form. Even if it is argued that in many Accident and Emergency situations the ten-day rule should be automatically overridden it would seem prudent to accept the rule as a formal statement of policy.

In a review article with regard to radiation effects on prenatal development (Mole, 1979) the summary asks whether, in the light of natural and radiation-induced risk estimates, the measures intended to reduce the possibility of exposure of the developing embryo or fetus are justified.

May I suggest that the "ten-day rule" has now acquired a status greater than that simply intended to reduce the possibility of irradiation of an early pregnancy?

Yours, etc.,
M. L. RAMSDALE.

Department of Medical Physics,
Leeds General Infirmary,
Leeds LS1 3EX.
(*Received March 1981*)

REFERENCES

Code of Practice for the Protection of Persons against Ionizing Radiations arising from Medical and Dental Use. 1972 (HMSO, London).

MOLE, R. H., 1979. Radiation effects on pre-natal development and their radiological significance. *British Journal of Radiology*, 52, 89–101.

A "new line" in radiology

THE EDITOR—SIR,

Since 1911, when Shenton described the radiological alterations in the hip in cases of tuberculosis (Shenton, 1911), all radiologists have used Shenton's line when diagnosing pathological conditions of the hip (Fig. 1).

The aim of this communication is to draw attention to a similar line we have found in the shoulder joint. This line can be identified not only on frontal, but also on lateral views. On the frontal view (Fig. 2) the line follows the lateral border of the scapula, the neck and the medial border of the humerus, and on the lateral view (Fig. 3) the line follows the lateral border of the scapula, the neck and the posterior surface of the humerus. In the presence of pathology a discontinuity of this line may be seen (Figs. 4 and 5). A similar line has been described in the frontal plane in a study of patients with hemiparesis (Bats, 1976). Our clinical colleagues have found this line particularly useful when reading films in the Casualty Department.

Yours, etc.,
A. KARLE,
E. B. HANSEN.

Department of Radiology,
Hvidovre Hospital,
University Hospital of Copenhagen,
DK-2650 Hvidovre, Denmark.
(*Received January 1981*)

REFERENCES

BATS, M. DE, 1976. La subluxation inferieure de l'épaule chez l'hemiplégué. *Annales de Médecine Physique*, 17, 185–213.

SHENTON, E. W. H., 1911. *Disease in Bone and its Detection by the X-rays* (Macmillan, London), pp. 42–43.

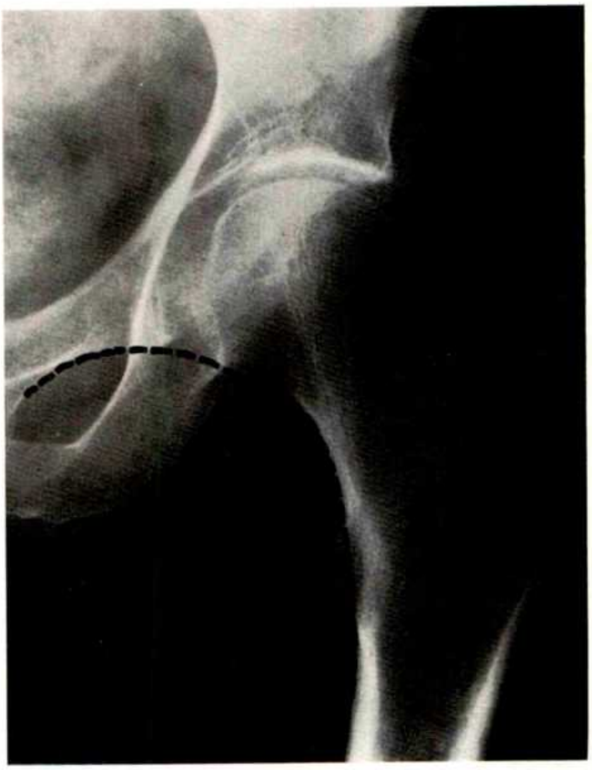


FIG. 1.

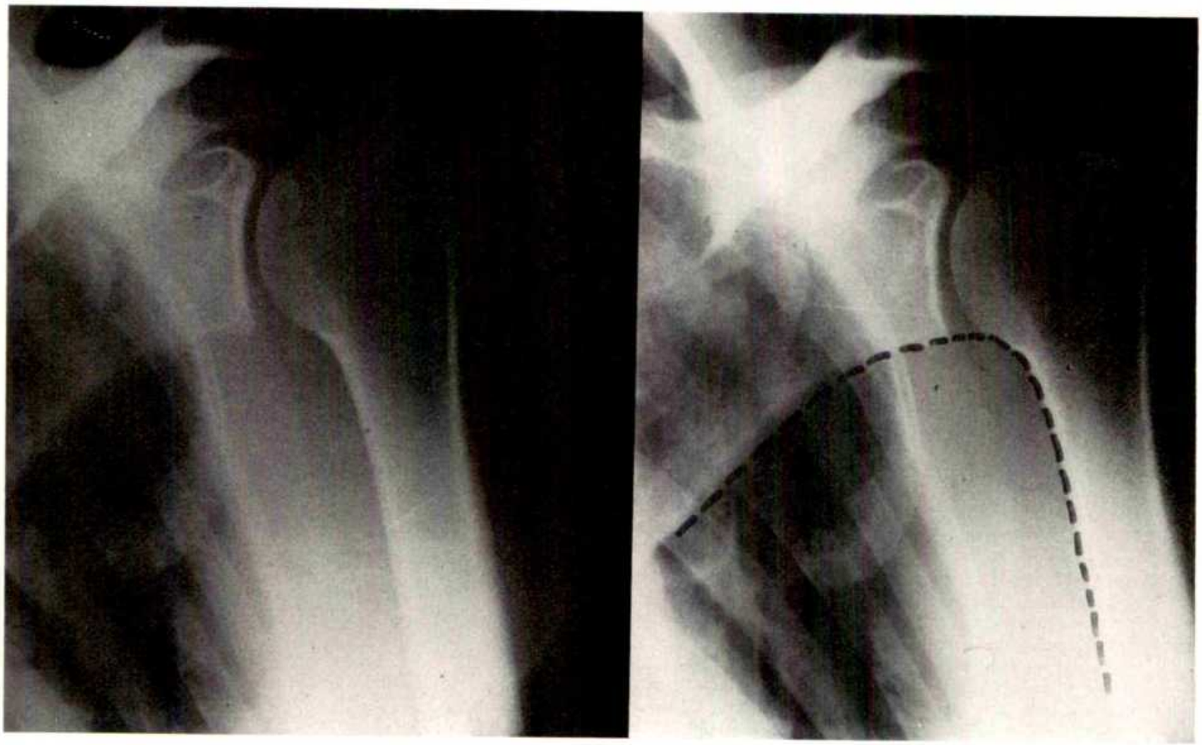


Fig. 2.

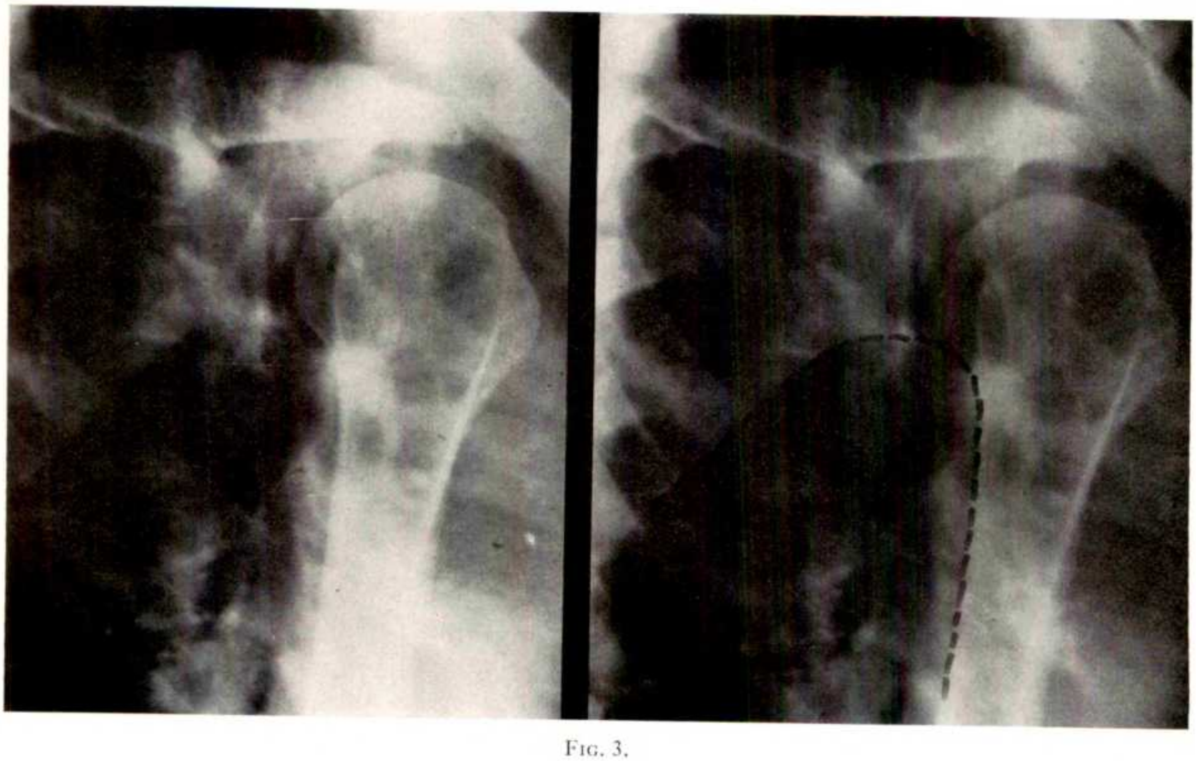


Fig. 3.

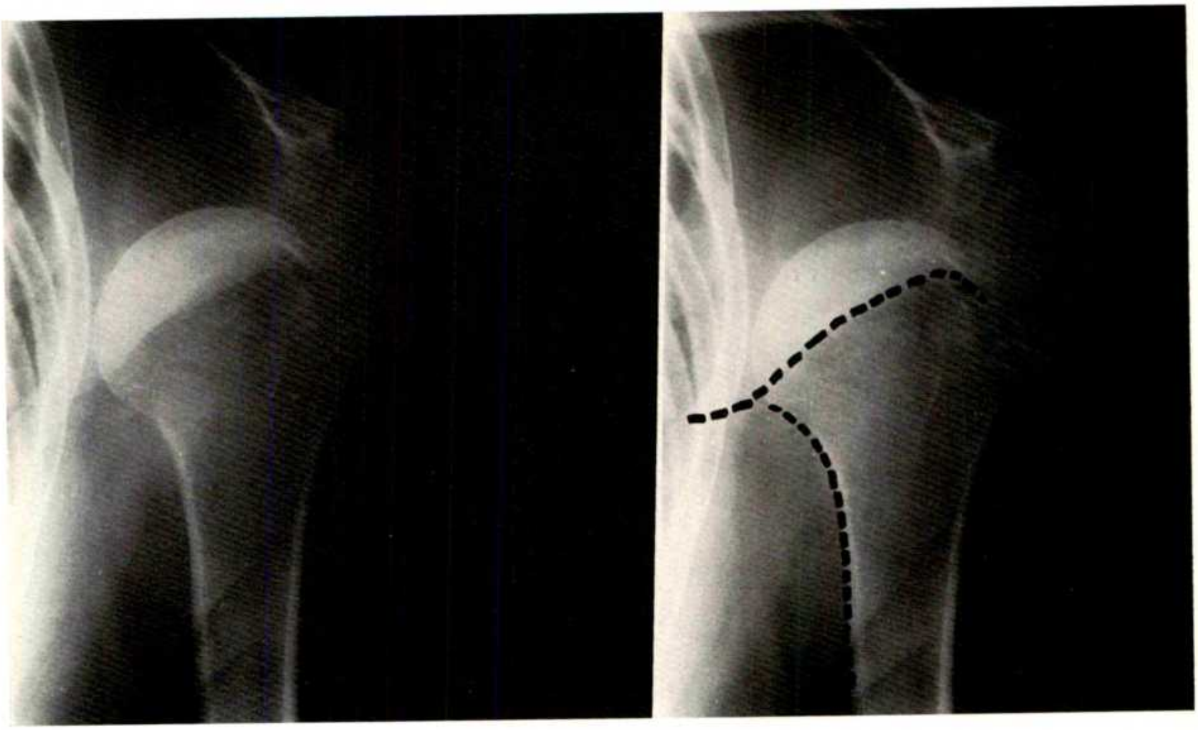


FIG. 4.

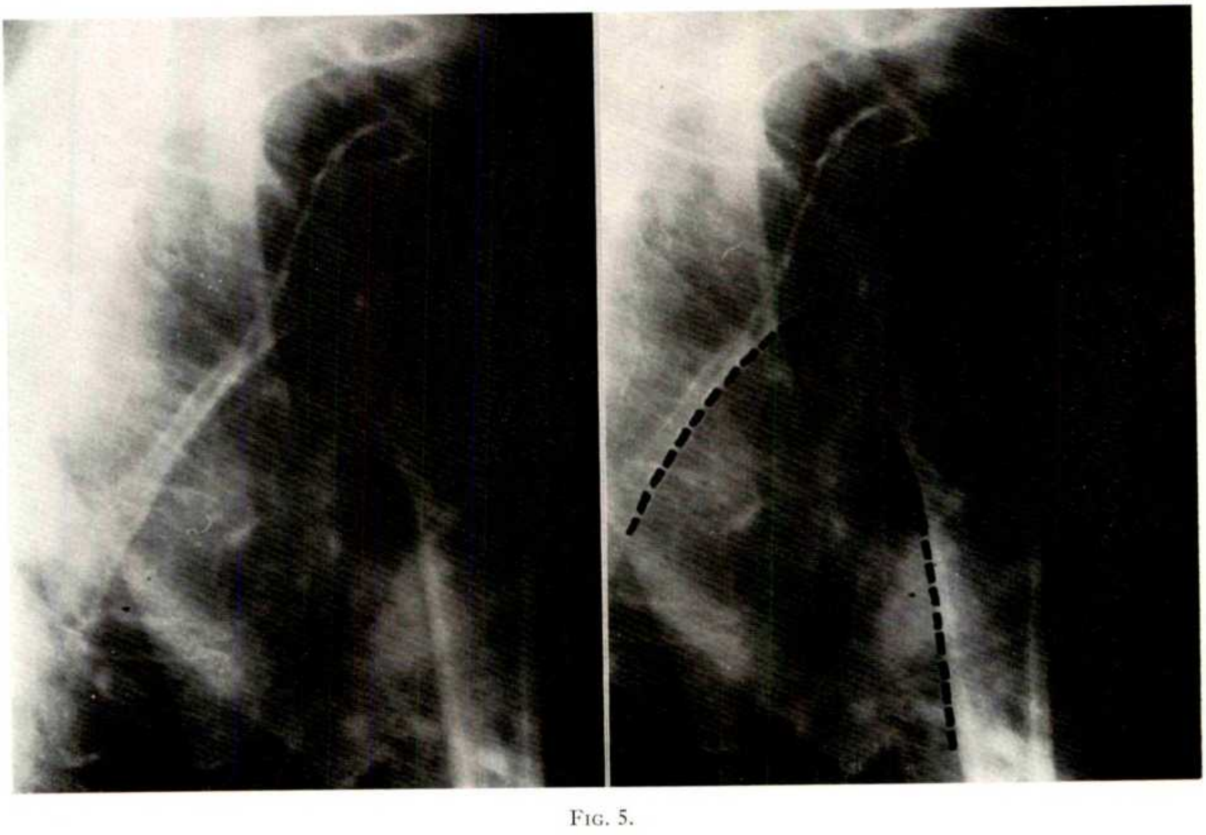


FIG. 5.

The incidence of headache following various techniques with metrizamide myelography

THE EDITOR—SIR,

The conclusions reached by Rolfe and Maguire (1980), that needle size and weight of iodine injected have no influence on the incidence of side effects, run contrary to first principles and to general experience. Fewer complications can be expected with the use of thinner needles and whilst perhaps not statistically significant in their series, is certainly clearly demonstrated by Tourtellotte *et al.* (1972) as quoted in the article. In a randomized double blind clinical trial comparing the 22 versus 26 gauge needle in the production of post-lumbar puncture syndrome in normal individuals, they recorded headaches in 32% and 12% of cases respectively. By using fine needles, complications are reduced in other radiological procedures such as percutaneous cholangiography and biopsy.

The position of the patient after lumbar puncture may be all important and patients who lie prone are very much less liable to headache. Also important is the size of the dural tear through which the cerebrospinal fluid leaks and it can be minimized by inserting the needle in the plane of the dural fibres, most of which run longitudinally (*British Medical Journal*, 1975).

Sound pharmacological principles dictate the use of the lowest possible concentration with the smallest quantity of contrast medium to produce acceptable diagnostic results. Rapid completion of the examination and subsequent removal of the drug, if possible, is also desirable. Hurwitz *et al.* (1980) found that 66% of the injected metrizamide could be aspirated after lumbar myelography and claimed that headaches and nausea were thereby reduced.

The application of the following principles in lumbar myelography will minimize its discomfort and complications and enable most to be done on an out-patient basis (van Niekerk, 1979).

1. Use the thinnest needle which is effective (22G in most cases). Local anaesthetic is not required when thin needles are used.
2. Insertion of the needle with the bevel in the plane of the dural fibres.
3. Avoid multiple punctures. To ensure accurate placement of the needle I prefer to do the lumbar puncture under screening control with the patient prone and with a pillow under the stomach.
4. Use the smallest effective quantity of contrast medium.
5. Minimize movement of the patient and rapidly complete the examination. There is thus less mixing of the contrast medium with the cerebrospinal fluid allowing optimal subsequent aspiration of the contrast medium.
6. Thereafter the patient should sit or remain semi-erect for an hour or two to allow absorption of much of the remaining small quantity of contrast medium and then lie prone to minimize leak of cerebrospinal fluid through the dural tear.

Yours etc.
J. P. DE V. VAN NIEKERK.

Department of Radiology,
Groote Schuur Hospital,
University of Cape Town,
South Africa.

(*Received February 1981*)

REFERENCES

BRITISH MEDICAL JOURNAL, 1975. Lumbar puncture (Editorial). *British Medical Journal*, *i*, 3.

HURWITZ, S. R., SUYDAM, M. and STEINBERG, A., 1980. Aspiration of metrizamide following lumbar myelography. *Radiology*, *136*, 789–790.

ROLFE, E. B. and MAGUIRE, P. D., 1980. The incidence of headache following various techniques of metrizamide myelography. *British Journal of Radiology*, *53*, 840–844.

TOURTELLOTTE, W. W., HENDERSON, W. G., TUCKER, R. P., GILLAND, O., WALKER, J. E. and KOKMAN, E., 1972. A randomized double blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post lumbar puncture syndrome in normal individuals. *Headache*, *12*, 73–78.

VAN NIEKERK, J. P. DE V., 1979. Myelography using water-soluble contrast media as an outpatient procedure. *South African Medical Journal*, *55*, 550–551.

(*Author's reply*)

THE EDITOR—SIR,

The needle gauges used in this study were those most commonly employed by radiologists performing frequent myelographic examinations. The incidence of headache was similar to that reported by other workers using similar calibre needles and differing doses of metrizamide and different water soluble contrast agents (Grainger *et al.*, 1976; Hindmarsh, 1975; Irstan and Sellden, 1976; Skalpe, 1977).

Tourtellotte *et al.* (1964) failed to show any significant difference in the frequency of post-lumbar puncture headache following the use of 18 gauge and 20 gauge spinal needles. This study, together with our own work and later series by Tourtellotte *et al.* (1972), indicates that needles of 24 or 26 gauge are required to achieve a significant reduction in the incidence of headache. The use of such needles is more time consuming and would make attempted aspiration of residual contrast agent, a procedure which is probably applicable only to examinations limited to the lumbar region, more tedious and presumably, as a consequence, less complete.

Our failure to demonstrate a relationship between the dosage of contrast medium and frequency of headaches may not be so surprising since all dosages were less than the manufacturers' recommended maximum. Other studies have also failed to show obvious connection (Cook and Wise, 1979) or very little significant relationship (Ahlgren, 1975) between these parameters.

The position adopted after lumbar puncture may be of importance. Brocker (1958) claimed to have virtually eliminated post-lumbar puncture headache by positioning the patient prone immediately after lumbar puncture which was performed using 18 gauge needles in all patients. Unfortunately a prone, horizontal position may not be adopted following myelography with water soluble contrast agents.

We have grave reservations on the performance of metrizamide myelography as an out-patient procedure. The most serious complication following the intrathecal use of metrizamide is seizure. Recently, Roper *et al.* (1979) studied EEG recordings in a group of 61 patients before and after metrizamide myelography. In this series of patients, six developed EEG changes over 24 hours after myelography, the intervening recordings having been entirely normal.

It has also been shown (Speck *et al.*, 1978) that there exists wide variation in the degree of persistence of water soluble contrast media within the cerebrospinal fluid in different patients. This finding is of some interest, particularly in view of the fact that one patient of van Niekerk's (1979) series of patients who underwent myelography as an out-patient procedure did in fact experience a seizure 14 hours after myelography despite apparent removal of metrizamide. This patient was an epileptic receiving treatment, though this fact was not appreciated at the time of the examination.

We therefore feel that until new, less epileptogenic water soluble contrast agents become available, there is no place in present radiological practice for out-patient myelography.

Yours etc.,
E. B. ROLFE.

Department of Radiology,
The Queen Elizabeth Hospital,
Birmingham.

(*Received April 1981*)

REFERENCES

AHLGREN, P., 1975. Amipaque myelography. The side effects compared with Dimer-X. *Neuroradiology*, *9*, 197–202.

BROCKER, R. J., 1958. Technique to avoid spinal tap headache. *Journal of the American Medical Association*, *168*, 261–263.

COOK, P. L. and WISE, K., 1979. A correlation of the surgical and radiculographic findings in lumbar disc herniation. *Clinical Radiology*, *30*, 671–682.

GRAINGER, R. G., KENDALL, B. E. and WYLIE, I. G., 1976. Lumbar myelography with metrizamide—a new non-ionic contrast medium. *British Journal of Radiology*, *49*, 996–1003.

HINDMARSH, T., 1975. Lumbar myelography with meglumine iocarmate and metrizamide. *Acta Radiologica*, *16*, 209–222.

IRSTAN, L. and SELLDEN, W., 1976. Adverse effects of lumbar myelography with Amipaque and Dimer-X. *Acta Radiologica Diagnosis*, *17*, 145–148.

ROPER, A. H., CHIAPPA, K. H. and YOUNG, R. R., 1979. Effect of metrizamide on EEG, a prospective study in 66 patients. *Annals of Neurology*, *6*, 222–226.

SKALPE, I. O., 1977. Adverse effects of water soluble contrast media in myelography, cisternography and ventriculography. *Acta Radiologica Supplementum*, *355*, 359–370.

SPECK, U., SCHMIDT, R., VOLKHARDT, V. and VOGELSANG, H., 1978. The effects of position of patients on the passage of metrizamide (Amipaque), meglumine iocarmate (Dimer-X) and ioserinate (Myelografin) into the blood after lumbar myelography. *Neuroradiology*, *14*, 251–256.

TOURTELLOTTE, W. W. HAERER, A. F., HELLER, G. L. and SOMERS, J. E., 1964. *Post Lumbar Puncture Headaches* (Charles C. Thomas, Springfield, Illinois), p. 87.

TOURTELLOTTE, W. W., HENDERSON, W. G., TUCKER, R. P. and GILLAND, O., 1972. A randomized double blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post lumbar puncture syndrome in normal individuals. *Headache*, *12*, 73–78.

VAN NIEKERK, J. P. DE V., 1979. Myelography using water soluble contrast media as an out-patient procedure. *South African Medical Journal*, *55*, 550–551.

Blood flow rate determination using computed tomography

THE EDITOR—SIR,

The recent article by Tonge *et al.* (1980) discussed a method to measure blood flow rate using computed tomography. In their discussion of limitations, they omitted a potentially serious one which could invalidate the technique.

The authors carefully calibrated their system *in vitro* and then showed its accuracy for measuring flow rate. However, these calibrations will not apply to the *in vivo* situation. The change in the effective energy of the X-ray beam *in vivo* due to the variation in size and composition of the body at each level scanned is totally unpredictable (Zatz and Alvarez, 1977). The calibration would have to be done *in vivo* at the level scanned. Since the calibration must be an internal one (Brooks *et al.*, 1980), this would require a second catheter in the vessel below the injection site to obtain samples for the calibration. Once the catheter was in place, CT would no longer be necessary since a standard indicator-dilution study could be done. The only time that the addition of CT might be useful would be to determine flow patterns in vessels other than the aorta which were included in the CT section and which branched from the aorta below the injection point.

Yours, etc.,
L. M. ZATZ.

Chief, Radiology Service,
VAMC and Professor of Radiology,
Stanford University School of Medicine,
Radiology Service (114),
VAMC,
Palo Alto, CA 94304, USA.

(*Received January 1981*)

REFERENCES

BROOKS, R. A., KELLER, M. R., O'CONNOR, C. M. and SHERIDAN, W. T., 1980 Progress toward quantitative computed tomography. *IEEE Transactions Nuclear Science*, *NS-27*, 1121–1127.

TONGE, K. A., WRIGHT, C. H., MATHEW, J., LEACH, R. D., and SAUNDERS, J. E., 1980. Flow rate determination using computed tomography. *British Journal of Radiology*, *53*, 946–949.

ZATZ, L. M. and ALVAREZ, R. E., 1977. An inaccuracy in computed tomography: the energy dependence of CT values. *Radiology*, *124*, 91–97.

(*Authors' reply*)

THE EDITOR—SIR,

In his letter Dr. Zatz has quite rightly pointed out that the effects of beam hardening would be unpredictable if this technique were used *in vivo* due to normal variations in human form. We recognized this as a problem and have found errors of the order of ±10% in the measurement of iodine concentration *in vitro* with our EMI 5005 Scanner. The phantom used simulated an anatomical cross section of the thorax with areas representing lung and bone as well as soft tissue. The dimensions of these structures and the density of the bone-like material were then severely varied.

Given these results we think that there are some regions of the body where the errors due to this problem may not be a handicap. The knowledge that more accurate and specific machines are being developed lead us to publish this rather fundamental experiment.

Yours, etc.,
K. A. TONGE.
On behalf of the authors.

St. Thomas' Hospital,
London SE1 7EH.

(*Received April 1981*)

The Dalkon Shield

THE EDITOR—SIR,

I wondered if I could seek the help of readers of your Journal with regard to women who still have the Dalkon Shield *in situ*. This intrauterine contraceptive device was removed from the market in 1975 after reports of sepsis and deaths from septic abortion in the United States. I am in the process of attempting to trace women at the London Hospital who had these inserted and in one case we found that the woman had had an IVU done last year where the Dalkon Shield is clearly shown (Fig. 1). This, however, was not noted by the trainee radiologist and many younger doctors may not be aware of the appearance or history of these dangerous contraceptive devices.

Recently the manufacturers circulated doctors with the recommendation that the shield should be removed from any woman in which it was still in place, citing the higher incidence of actinomycosis in women with long term use. Recent work in the United States has shown that the tail of this device undergoes biodegradation and it is likely that

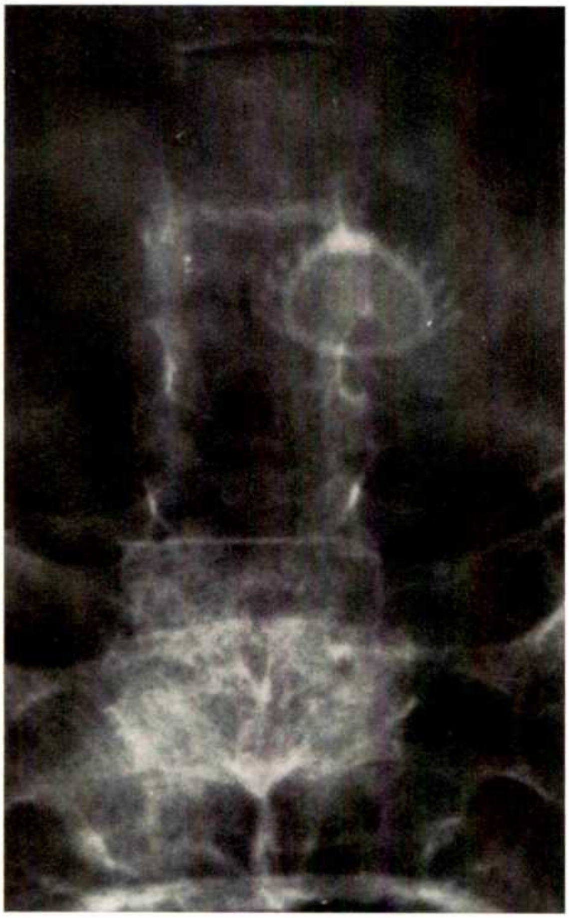


FIG. 1.

increasing rates of sepsis will be encountered with long term use.

One hundred thousand of the Dalkon Shields were sold in this country and there has never been a formal recall system. From the interim results of our study in Tower Hamlets it seems that between 10% and 15% of the women fitted with the shield may still have it in place and I would like to draw this to your readers' attention and ask them to alert the clinician concerned so that he can arrange for this shield to be removed by the appropriate specialist.

Yours, etc.,
W. D. SAVAGE.

Department of Obstetrics & Gynaecology,
The London Hospital (Mile End),
Bancroft Road, London E1 4DG.
(*Received April 1981*)

Migration of localizing wire into pleural cavity

THE EDITOR—SIR,

I was interested to read of the case reported (Bristol and Jones, 1981) where a Frank localizing wire inserted into a suspect area in a breast had migrated into the pleural cavity.

This possibility caused us some anxiety when we first commenced to localize breast lesions for biopsy by this method. Consequently, we have adopted the simple expedient of bending the protruding end of the localizing wire through a right angle at skin level, a technique we commend to your readers.

Technically, once the wire has been inserted it is firmly held by a Spencer Wells forceps at skin level. A second Spencer Wells is applied a couple of millimetres above the first and this is twisted until the exposed portion of the wire lies parallel to the skin. A small gauze dressing is passed between the wire and the skin to avoid the possibility of the tip scratching the patient. The whole is secured by a micropore dressing and films using compression are taken in supero-inferior and lateral projection.

Since adopting this technique we have experienced no problems with wire migration even though over 80 of our patients have travelled by car or taxi to another hospital some four miles distant, and seven have travelled over 15 miles to another town, all with a marker *in situ*.

Yours, etc.,
E. J. ROEBUCK.

University Hospital,
Nottingham.
(*Received February 1981*)

REFERENCE

BRISTOL, J. B. and JONES, P. A., 1981. Migration of localizing wire into pleural cavity. *British Journal of Radiology*, *54*, 139–140.

THE EDITOR—SIR,

I have read with interest the recent article concerning transgression of a localizing wire used for pre-operative percutaneous localization of non-palpable breast lesions (Bristol and Jones, 1981). Unfortunately the statement by the authors that the technique was previously free of reported complications is unwarranted. For some reason their review of the literature failed to identify a recent paper appearing in 1979 regarding migration of the hooked localization wire. Not only is it mandatory to stabilize the external end of the wire, but as I reported in this paper it is insufficient to stabilize it with anything but a strong screw-clamp device.

Yours, etc.,
M. J. HOMER.

Mammography Section,
Department of Radiology,
Box 388,
Tufts-New England Medical Center,
171 Harrison Avenue,
Boston, MA 02111 USA.
(*Received March 1981*)

REFERENCES

BRISTOL, J. B. and JONES, P. A., 1981. Transgression of localizing wire into the pleural cavity prior to mammography. *British Journal of Radiology*, *54*, 139–140.
HOMER, M. J., 1979. Percutaneous localization of breast lesions: experience with the Frank breast biopsy guide. *Journal of the Canadian Association of Radiologists*, *30*, 238–241.

(*Author's reply*)

THE EDITOR—SIR,

The events reported in our article (Bristol and Jones, 1981) occurred in February 1979 and the report was prepared later that year. At the time of preparation our literature search did indeed fail to identify Dr. Homer's paper, probably because it was published in December 1979 and would not have been cited until well into 1980.

The need to guard the wire end is endorsed in both papers, although the nature of the guard may surely vary as long as it is secure.

We thank Dr. Roebuck for his observations. We have also employed the technique of bending the external tip of the wire and found this reasonably satisfactory, but are also at present experimenting with the use of Denis Browne aluminium collars which can be squeezed on the the end of the wire after final positioning and are relatively unobtrusive.

Yours, etc.,
J. B. BRISTOL.

Department of Surgery,
Bristol Royal Infirmary.
(*Received April 1981*)

REFERENCES

BRISTOL, J. B. and JONES, P. A., 1981. Transgression of localizing wire into the pleural cavity prior to mammography. *British Journal of Radiology*, *54*, 139–140

HOMER, M. J., 1979. Percutaneous localization of breast lesions: experience with the Frank breast biopsy guide. *Journal of the Canadian Association of Radiologists*, *30*, 238–241.

Para-aortic nodes in carcinoma of the cervix

THE EDITOR—Sir,

I fear that Dr. J. S. Macdonald cannot have spoken to his radiotherapist colleagues before writing his book review on the *Atlas of Lymphography* by Viamonte and Ruttimann (*British Journal of Radiology*, 1981, *54*, p.270) in which he states "the stress laid on the involvement of the para-aortic nodes in carcinoma of the cervix and body of the uterus is very important, since this is not widely realised and many deaths could be prevented by lymphography and adequate treatment in these patients."

Radiotherapists and gynaecologists dealing with these diseases are very aware of the frequency of para-aortic lymph-node metastases; however, for reasons equally well-known to radiotherapists, nobody has yet been able to show that treatment of these nodes adds significantly to the likelihood of cure. The few patients who might benefit—and this is difficult to prove—are those with clinically early primary tumours and micrometastases in the para-aortic chain, which of course are not demonstrable by lymphography.

Yours etc.,
I. J. KERBY.

Department of Radiotherapy and Oncology,
Velindre Hospital,
Whitchurch,
Cardiff CF4 7XL.
(*Received March 1981*)

(*Author's reply*)

THE EDITOR—SIR,

I have read Dr. I. J. Kerby's letter with interest. I should like to assure him that I not only speak to my radiotherapy colleagues but work very closely with them.

To quote the experience of one of my radiotherapy colleagues Dr. Joan Baker: in her series of patients with cancer of the cervix 22 were shown at lymphography to have involved para-aortic nodes; nine of these patients are alive and well, three between three and five years, six over five years. None of the remainder recurred in the para-aortic nodes after radiotherapy and deaths were due to inability to control primary disease. I would submit that it is important to know if these nodes are involved because from these figures they are obviously eminently treatable if they are found before they are too large. As for micro-metastases, we will of course never show these, but if lymphography is used properly with adequate follow-up films then as soon as micro-metastases become macro-metastases they can be seen and treated. One of these long-term survivors showed radiologically normal nodes at the time of lymphography but developed an obvious para-aortic deposit during follow-up. This was irradiated and there has been no evidence of recurrence of disease.

I still doubt whether in general radiotherapists and oncologists dealing with this disease are aware of the frequency of para-aortic node involvement, and also how eminently treatable these nodes are when the diagnosis is made when the amount of disease present is still small.

Yours etc.,
J. S. MACDONALD.

Diagnostic X-ray Department,
The Royal Marsden Hospital,
Downs Road,
Sutton, Surrey SM2 5PT.
(*Received April 1981*)

Radiation hazards

THE EDITOR—SIR,

In his Sylvanus Thompson Memorial Lecture Sir Richard Doll (1981) discusses, among other important matters, the effects of irradiation *in utero*. He uses Mole's (1974) analysis of the findings for twins from the Oxford Childhood Cancer Survey to support the conclusion that exposure to diagnostic X rays *in utero* causes an enhanced risk of malignancy during childhood. Doll believes that it is "reasonable to ignore" the alternative hypothesis that mothers who are selected for X-ray examination on medical grounds tend, by virtue of their constitution, to bear children who are more vulnerable to childhood malignancies. However, in common with Mole, he fails to point to a striking paradox in the data for twins and to evaluate statistical errors.

If death-rates from leukaemias and solid cancers during the first ten years of life are calculated for the entire populations (irradiated and unirradiated combined), first of singletons and then of twins, we find that the rates in twins (both monozygotic and dizygotic) were slightly, but not significantly, *lower* than in singletons. (The rates, ±SE, for childhood leukaemias were $(2.35 \pm 0.04) \times 10^{-4}$ in singletons and $(1.98 \pm 0.27) \times 10^{-4}$ in twins; those for solid cancers were $(2.75 \pm 0.04) \times 10^{-4}$ in singletons and $(2.58 \pm 0.27) \times 10^{-4}$ in twins.) Considering that 55% of twins were irradiated *in utero* in contrast to only 10% of singletons—leading us to expect that rates of childhood malignancies in twins would be about 20% higher than in singletons—these findings are not readily accommodated to the causal view. On the other hand, and consistent with the causal interpretation, the relative risks (irradiated versus unirradiated) appear to be similar in singletons and twins. However, when we calculate the errors in the estimated relative risks we discover that the data for twins are, for present purposes, essentially uninformative. From the data in Mole's (1974) Table 1 the relative risk of leukaemias in twins (irradiated versus unirradiated) works out at 2.20 with 95% confidence limits of 1.34 and 4.17, as compared with 1.56 (limits 1.41 and 1.71) in singletons; for solid cancers the corresponding relative risks were 1.58 (limits 1.04 and 2.57) in twins and 1.50 (limits 1.37 and 1.63) in singletons. That is to say, the estimated relative risks for twins have such wide error limits that they cannot be used legitimately to support the causal hypothesis.

On another but closely related issue Totter (1980) contends that, when the full Oxford Survey data (Stewart and Kneale, 1970) are analysed in the "usual way" to relate excess malignancies to radiation dose, no significant correlation is obtained.

So far as I am aware the only study free from the complications of medical selection that has sufficient statistical power to bear directly and critically on the causal versus selection alternatives is that of the 1292 children who were irradiated *in utero* by the nuclear bombs at Hiroshima and Nagasaki (Jablon and Kato, 1970). The number of childhood malignancies expected at Japanese national death-rates was 0.75; the excess deaths from all childhood malignancies expected on a simple linear extrapolation of Stewart and Kneale's (1970) original dose-response relation was 36.9. Only one death from a childhood malignancy was recorded. Although plausible justifications can be advanced for lowering the original estimate of 36.9, the gap between it and 0.25 is not easy to bridge. Subtle selection factors related to distance from the hypocentre might have biassed the outcome but medical selection was not a complication.

It is prudent to act as though antenatal irradiation increases the risk of childhood malignancies but we should not assume that the phenomenon has been established by valid scientific procedures.

Yours etc.,
P. R. J. BURCH.

Department of Medical Physics,
University of Leeds,
The General Infirmary,
Leeds LS1 3EX.
(*Received March 1981*)

REFERENCES

DOLL, R., 1981. Radiation hazards: 25 years of collaborative research. *British Journal of Radiology*, *54*, 179–186.

JABLON, S. and KATO, H., 1970. Childhood cancer in relation to prenatal exposure to atomic-bomb radiation. *Lancet*, *ii*, 1000–1003.

MOLE, R. H., 1974. Antenatal irradiation and childhood cancer: causation or coincidence? *British Journal of Cancer*, *30*, 199–208.

STEWART, A. M. and KNEALE, G. W., 1970. Radiation dose effects in relation to obstetric X-rays and childhood cancers. *Lancet*, *i*, 1185–1188.

TOTTER, J. R., 1980. Some observational bases for estimating the oncogenic effects of ionizing radiation. *Nuclear Safety*, *21*, 83–94.

The relationship of dose to prognosis in squamous cell carcinoma of the aerodigestive tract

THE EDITOR—SIR,

The paper by Wollin and Kagan (1981) with this title gives me cause for concern. Essentially, the authors found little or no correlation between tumour cure rates and the ret doses received by tumours treated with different fractionation regimes.

Although it is not stated precisely by the authors, the ret doses appear to have been calculated using the normal-tissue NSD formula of Ellis (1966), *i.e.*

$$\text{Normal tissue NSD} = \text{total dose} \times N^{-0.24} \times T^{-0.11} \qquad (1)$$

where N is the number of fractions and T is the overall treatment time. In fact, Ellis (1969) used the following formula for tumours:

$$\text{Tumour NSD} = \text{total dose} \times N^{-0.24} \quad . \quad . \qquad (2)$$

If five fractions per week are employed, equation (2) would give ret values 31% higher for ten fraction regimes and 72% higher for 100 fraction regimes than the ret doses calculated using equation (1).

The Ellis formulae were based on the average slopes of the isoeffect curves for early and medium-term skin and quamous-cell carcinoma reactions over the range one to 30 "daily" fractions. The curves were obtained by plotting isoeffect dose against overall treatment time on a log-log scale. The slopes so obtained are very dependent on the precise definition of overall treatment time as discussed by Liversage (1971) and in more detail by Liversage and Dale (1978).

The paper by Wollin and Kagan appears to include regimes involving as many as 100 fractions; *e.g.* Andrews (1965) is quoted as giving total doses of 10000 cGy (rad) using daily doses as low as 98 cGy (rad). This is far outside the range of the data from which the Ellis formulae were derived.

Experimental and clinical evidence from Douglas *et al.* (1975) and Dutreix *et al.* (1973) on skin reactions suggests that the slope of the isoeffect curve, obtained by plotting the logarithm of isoeffect dose against the logarithm of the number of fractions, decreases rapidly as the number of fractions exceeds 15 or 30. Dutreix *et al.* (1973) suggests that the curve may become horizontal above about 30 fractions. If this is so, the exponent of N in the Ellis NSD formulae would reduce to zero for values of N greater than 30. Should such a reduction in the slope of the isoeffect curve occur in the case of the tumours considered by Wollin and Kagan, the ret doses as calculated by equation (2) would be 30% lower for regimes employing 100 fractions than they would be for isoeffect regimes employing 30 fractions.

In view of the above uncertainties, it is not in the least surprising that Wollin and Kagan found little or no correlation between their calculated ret doses and tumour cure rates. I believe that for a given treatment regime the magnitude of the dose delivered to the tumour can be critical and that radiotherapists and physicists should be encouraged to improve still further the accuracy of their dosimetry.

The lack of correlation between ret doses and tumour cure reported by Wollin and Kagan indicates to me that there is simply a lack of correlation between the isoeffect curve predicted by the NSD formula used by these authors and the true isoeffect curve.

Nobody knows the true shape of the isoeffect curve for the tumours discussed above but Wollin and Kagan could perhaps use the large amount of data they have collected in an attempt to determine the approximate shape of this curve for daily fractionation regimes.

Yours, etc.,
W. E. LIVERSAGE.

Radiation Physics Department,
St. Bartholomew's Hospital,
London EC1A 7BE.
(*Received February 1981*)

REFERENCES

ANDREWS, J. R., 1965. Dose–time relationships in cancer radiotherapy: a clinical radiobiology study of extremes of dose and time. *American Journal of Roentgenology*, *93*, 56–74.

DOUGLAS, B. G., FOWLER, J. F., DENEKAMP, J., HARRIS, S. R., AYRES, S. E., FAIRMAN, S., HILL, S. A., SHELDON, P. W. and STEWART, F. A., 1975. The effect of mutiple small fractions of X rays on skin reactions in the mouse. In *Cell Survival after Low Doses of Radiation* (The Institute of Physics and John Wiley and Sons Ltd., England), pp.351–361.

DUTREIX, J., WAMBERSIE, A. and BOUNIK, C., 1973. Cellular recovery in human skin reactions: application to dose fraction number overall time relationship in radiotherapy. *European Journal of Cancer*, *9*, 159–167.

ELLIS, F., 1969. Dose, time and fractionation: a clinical hypothesis. *Clinical Radiology*, *20*, 1–7.

LIVERSAGE, W. E., 1971. A critical look at the ret. *British Journal of Radiology*, *46*, 91–100.

LIVERSAGE, W. E. and DALE, R. G., 1978. Dose–time relationships in irradiated weevils and their relevance to mammalian systems. In *Current Topics in Radiation Research*, *13* (North Holland Publishing Co., Amsterdam), pp. 97–187.

WOLLIN, M. and KAGAN, A. R., 1981. The relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract. *British Journal of Radiology*, *54*, 36–39.

Correspondence

(*Authors' reply*)

THE EDITOR—SIR,

Dr. Liversage's letter eloquently raises many of the issues with which we tried to grapple in our paper. The primary question we tried to answer was what role does dose, time, and fractionation play in curing cancer? Can we tell in percentage terms what its contribution is?

We found a low percentage contribution in the articles we studied. There are two main ways to question our methods. One is to question our statistical tests. The test we chose looks primarily at the ordering of the cases on any arbitrary scale you choose, whether normal tissue NSD, tumour NSD, or any other isoeffect formula you care to use. Thus the absolute value of NSD is not important, but whether all the cures are grouped around high values and the failures grouped around low values.

The other way to question our methods is to say a better isoeffect formula would show a higher correlation or order the data better. Perhaps, but our point is that no matter what formula you use there are still factors that affect outcome but which are not included in those dose, time and fractionation isoeffect formulae. Because these factors are not present in the formula, the correlation will be poor. We used normal-tissue NSD in our paper. The reason we did so is that the correlation did not change whether normal-tissue or tumour NSD was used.

Andrews (1965), for example, has two cases with 82 fractions and the rest with fewer. The majority of his cases (80%) received 45 fractions or fewer. There was no change in the correlation whether tumour NSD or normal-tissue NSD was used. Table I shows the comparison between the two for selected examples. If anyone wishes to try another isoeffect formula, we will gladly use it and subject it to our analysis.

We do not doubt that radiation cures cancer or that improved dosimetry will increase cure. After all, one author is a physicist and the other a radiation therapist. But we would like a proper appreciation of what effect we are actually having on the overall cure rate.

Yours, etc.,
M. WOLLIN,
A. R. KAGAN.

Radiation Therapy Department,
Southern California Permanente Medical Group,
Los Angeles,
California, USA.

(*Received May 1981*)

TABLE I

Source of data	RPB		RPB^2 (%)		Significance at 0.05 level	
	Normal tissue	Tumour	Normal tissue	Tumour	Normal tissue	Tumour
Fayos (1975)	−0.112	−0.130	1.2	1.7	NS	$p<0.05$
Shukovsky and Fletcher (1973)						
Tonsillar fossa, T1, T2	−0.004	−0.061	0	0	NS	NS
Tonsillar fossa, T3, T4	+0.225	+0.284	8.1	8.1	$p<0.05$	$p<0.05$
Tonsillar fossa, all stages	+0.120	+0.106	1.4	1.1	NS	NS
Andrews (1965)	+0.163	+0.166	2.7	2.8	NS	NS

For references and an explanation of the table see the original article: Wollin, M. S. and Kagan, A. R., 1981. The relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract. *British Journal of Radiology, 54*, 36–39.

Radiation doses in neutron therapy

THE EDITOR—SIR,

Dr. Hornsey's correspondence entitled "Appropriate RBEs for use in neutron therapy" (1980) correctly points out the hazard to normal tissue following the use of a "universal RBE of 3" to calculate equivalent doses of neutrons and photons in phase I and II clinical trials at the University of Washington. If one carries this concept to the next step, one arrives at the conclusion that neutron therapy was not superior to conventional therapy in treating head and neck cancer patients at the University of Washington. The reason for this, as shown in Fig. 1, is that if the RBEs are between four and five as determined radiobiologically, the total biologically effective doses in the mixed beam and all neutron schedules are significantly larger than the doses received by comparable patients who had T3, T4 head and neck lesions (often coupled with cervical adenopathy) and who were treated with photons during the same time span. In spite of these larger doses, there has been no significant improvement over photon therapy in the tumour response or in survival of the neutron-treated patients (Geraci, 1981a; Laramore *et al.*, 1979; 1980), except as reported in two publications (Griffin *et al.*, 1978; 1979). These two exceptions are reports in which errors were probably made by labelling neutron patients as mixed-beam patients (Geraci, 1981b). This is important since it is only the mixed beam option which is reported to give a significantly higher tumour-control rate than photon treatments. Therefore, the conclusion presented in these two papers needs to be re-evaluated.

The substantial increase in normal-tissue damage and the absence of comparable increase in local tumour control in these patients also suggests that the neutron dose-response curve for damage to normal tissue is steeper than the neutron dose-response curve for local tumour control. These results are not good omens for the efficacy of neutron therapy of advanced head and neck cancers.

Yours etc.,
J. P. GERACI.

Radiological Sciences,
University of Washington,
Seattle, Washington 98195, USA.

(*Received March 1981 and in revised form April 1981*)

REFERENCES

GERACI, J. P., 1981a. Efficacy of neutrons in radiotherapy. *Health Physics, 40*, 41–53.

1981b. A question in evaluation of mixed beam (neutron/photon) therapy. *European Journal of Cancer, 17*, 367.

GRIFFIN, T. W., LARAMORE, G. E., PARKER, R. G., GERDES,, A. J., HEBARD, D. W., BLASKO, J. C. and GROUDINE, M. T., 1978. An evaluation of fast neutron teletherapy of metastatic cervical adenopathy from squamous cell carcinomas of the head and neck region. *Cancer, 42*, 2517–2520.

GRIFFIN, T. W., BLASKO, J. and LARAMORE, G., 1979. Results of fast neutron pilot studies at the University of

1981, *British Journal of Radiology*, *54*, 700–701

Washington. In *High LET Radiations in Clinical Radiotherapy*, Ed. by G. W. Barendsen, J. J. Broerse and K. Breur (Pergamon Press, Oxford), pp.23–29.

Hornsey, S., 1980. Appropriate REBs for use in neutron therapy. *British Journal of Radiology*, *53*, 1207.

Laramore, G. E., Griffin, T. W., Tong, D., Groudine, M. T., Blasko, J. C., Kurtz, J., Russell, A. and Parker, R. G., 1980. Fast neutron teletherapy for advanced carcinomas of the oral cavity and soft palate. *Cancer*, *46*, 1903–1909.

Laramore, G. E., Blasko, J. C., Griffin, T. W. and Groudine, M. T., 1979. Fast neutron teletherapy for advanced carcinomas of the oropharynx. *International Journal of Radiation Oncology, Biology and Physics*, *5*, 1821–1827.

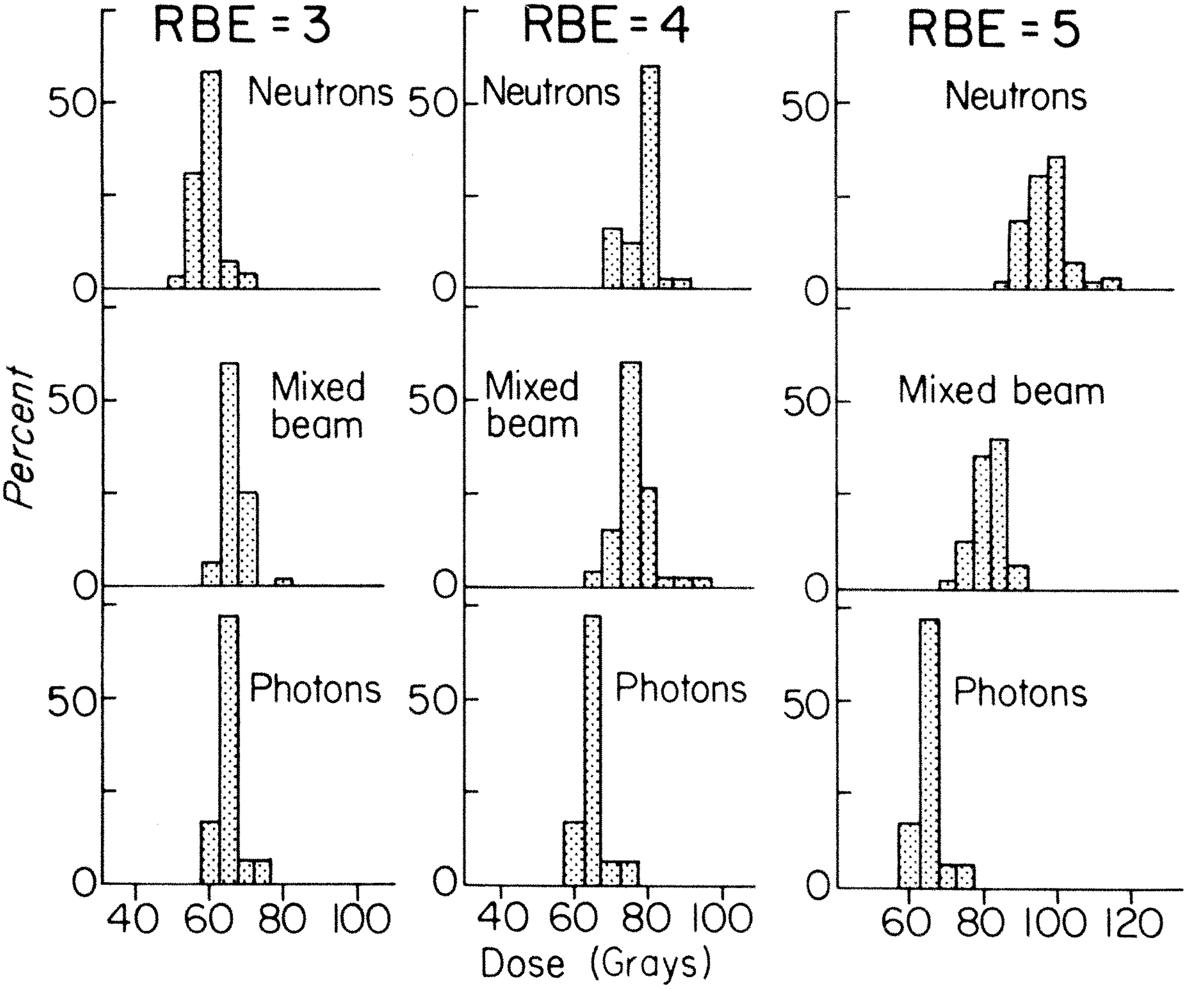


Fig. 1.

Percentage distribution of patients according to total radiation dose delivered following neutron (58 patients), mixed beam (47 patients), and photon (18 patients) treatments. Radiation doses of patients treated before May 1977 were obtained from the charts in the medical records department of the University Hospital. Patients treated with pre-operative radiation or neutron boost were excluded from this analysis. Patients had primary tumours of the oral cavity, oropharynx, hypopharynx, larynx and nasopharynx. The total photon-equivalent dose in Gy was calculated by multiplying the neutron dose by the indicated RBE and adding to it the photon dose.

(*Author's reply*)

The Editor—Sir,

Dr. Geraci's letter highlights the problems that arise in converting neutron doses to equivalent photon doses by using any conversion factor or RBE. Eventually there will be sufficient information on response to neutrons for thinking and working in neutron dose alone. If comparisons are made between chemotherapy and photon therapy no one thinks of using a conversion factor to compare their effectiveness. However, as damage to tissues by neutrons is similar to that by photons we can use the relevant information to avoid overtreating patients. To avoid overtreatment, the RBE relevant to the limiting normal tissue must be used but only for fields which include that limiting tissue.

The RBE of 5 previously proposed (Hornsey, 1980) at a photon dose of about 200 rad/fraction was for the CNS only and is therefore not appropriate for determining the tumour dose unless the tumour is in the CNS. We do not know the appropriate RBE for tumours but, clearly, if it is the same or less than that for the limiting normal tissue, there will be no improvement in tumour control. Dr. Geraci suggests that no improvement in local control was observed in the Seattle trial except in two reports. This suggests that the RBE for this mixed bag of tumours was not higher than that for the limiting normal tissues. The rationale for neutron therapy is that some tumours, because of hypoxia or other factors, will have a high RBE, higher than the limiting normal tissues, and the present clinical trials will, we hope, determine which these tumours are. Already, some tumours for which the radiation treatment of choice may be neutrons are becoming clear—tumours of the salivary glands and perhaps those of the floor of the mouth. The latter tumours are particularly relevant to the present discussion because a contributory factor to the excellent results obtained with neutrons is that the neutron dose, unlike the photon dose, is not so limited by late damage to the jaw bone. The RBE for damage to bone is low due to the low absorption of neutrons in bone.

In many ways it is misleading to use "equivalent dose" calculated by using an arbitrary RBE for comparing tumour doses. "Equivalent dose" is only useful in determining tolerance levels for normal tissues. The only relevant comparison for tumour response is the response obtained with different modalities for tolerable and equivalent damage to normal tissue.

Yours etc.,
SHIRLEY HORNSEY.

MRC Cyclotron Unit,
Hammersmith Hospital,
Du Cane Road,
London W12.
(*Received May 1981*)

REFERENCE

HORNSEY, SHIRLEY, 1980. Appropriate RBE's for use in neutron therapy. *British Journal of Radiology*, *53*, 1207.

Preparation for barium enema

THE EDITOR—SIR,

Many radiologists demand a period of semi-starvation for 24 or 36 hours prior to a barium enema examination. During this period only clear fluids may be taken.

Many patients find this difficult, in particular diabetics, the very old, and patients with active duodenal ulcers. There exist elemental diet mixtures which are designed to leave no bowel residue—the so-called astronaut diet. These are designed for a few specific clinical conditions but do not appear to be widely used by radiologists. The fat they contain is medium chain triglyceride which is wholly absorbed.

An example which has been found to be very satisfactory is Triosorbon, from BDH Pharmaceuticals Ltd. It is probably too expensive to be used as a routine preparation but is recommended for the groups mentioned above.

Yours, etc.,
J. G. B. RUSSELL.

X-ray Department,
Saint Mary's Hospital,
Whitworth Park,
Manchester M13 0JH.
(*Received May 1981*)

Calcification of the posterior longitudinal ligament of the spine

THE EDITOR—SIR,

Regarding the letter from Park and Mourad (1980), I agree that the condition may occur more widely than reported, and would like to mention a report of 26 cases in South India by my colleagues and myself (Deshpande *et al.*, 1976).

Yours, etc.,
I. DINAKAR.

Department of Neurosurgery,
Kurnool Medical College,
Kurnool, India.
(*Received April 1981*)

REFERENCES

DESHPANDE, R. P., DINAKAR, I. and SHANKAR REDDY, M., 1976. Calcified posterior longitudinal ligament and myelopathy. *Indian Journal of Orthopaedics*, *10*, 78–82.

PARK, W. M. and MOURAD, K., 1980. Ossification and calcification of the posterior longitudinal ligament of the spine. *British Journal of Radiology*, *53*, 375–376.

Obituary

John Dedrickson Frye

The death occurred at the end of February, 1981 of John Frye. He was 88 years old, a nephew of the late Cuthbert Andrews (maker of X-ray tubes and a past President of the BIR) and for over 30 years his technical designer.

John Frye was educated at St. Marylebone School and joined his uncle in 1915 when the small London X-ray tube factory of C. H. F. Müller of Hamburg was acquired from the Custodian of Enemy Property. He was involved in the problems of continuing manufacture of the existing models by the still largely German glassblowers and vacuum engineers and the development of the new "Mammoth" gas tube, produced in thousands for the War Department and other hospitals between 1915 and 1919. He then designed the "Leviathan" with a massive copper anti-cathode in an 8 in diameter glass bulb; this was the ultimate in "gas-tubes".

Between the wars, and after various patent disputes connected with the hot-cathode principle and the line-focus application of it, John Frye produced the "Protexray" tube, the only self-protected hot cathode tube of British manufacture ever to be commercially successful. About 1933 he developed it further as the "Isolex" shockproof tube which may well have been the first oil-immersed X-ray tube ever put on the market.

It was entirely due to John Frye's technical skill that this British-made X-ray tube was available in 1939 when Continental sources were in enemy hands and American convoys were to be so gravely threatened by submarine warfare.

He had been a widower for many years and his only daughter and son-in-law abandoned their life sailing the world and returned to care for him during the last few years of his life.

R.C.A.

1981, *British Journal of Radiology*, *54*, 702–713 August 1981

Proceedings of The British Institute of Radiology*

Radionuclides in gastroenterology

Abstracts of papers presented at a meeting held on Wednesday, February 18, 1981 at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG

Bile salts

Chairman: Dr. M. V. Merrick

Assessing small-intestinal function, by I. W. Percy-Robb. (*Introductory talk.*)
Radioisotopes in testing ileal function, by M. van Blankenstein, J. W. O. v. d. Berg, R. de Groot and H. Delhez.
Dynamic imaging of the entero-hepatic circulation with SeHCAT, by S. T. Meller, R. M. Kupfer, R. P. Jazwari, J. H. Payne, V. R. McCready and T. C. Northfield.
The detection of ileal disease with SeHCAT, by H. Nylhin, M. A. Eastwood and M. V. Merrick.
Detection of ileal dysfunction using SeHCAT, by Elizabeth A. Fagan, I. M. Baird and V. S. Chadwick.
Hepatic clearance of a radiolabelled bile acid as a test of liver function, by J. H. Marigold.

The proximal gut

Chairman: Dr. D. N. Croft

Gastric emptying revisited, by L. K. Harding.
Gastric emptying of solids, by R. C. Heading, S. Holt, J. Reid, T. V. Taylor and P. Tothill.
Interpretation of gastric emptying in patients with dyspepsia, by S. L. Grainger, Judith I. Gaunt, R. P. H. Thompson and D. N. Croft.
Gastric mucosal uptake of pertechnetate—controversy and clinical applications, by J. G. Williams.
Radioisotope milk scans in paediatrics, by I. Gordon.
Radionuclide transit studies of the oesophagus, by J. N. Blackwell, R. C. Heading, S. Holt, W. J. Hannan and P. Tothill.
Observations of $^{14}CO_2$ breath excretion patterns using an orally administered preparation of ^{14}C-labelled cellulose, by J. M. Findlay, G. C. Hart, T. Srinivasan, B. Selby and K. M. Davis.
The formation of functional images from the HIDA scan, by D. L. Hastings, R. W. Nicholson, R. A. Shields and H. J. Testa.
Clinical applications of functional images from the HIDA scan, by R. W. Nicholson, D. L. Hastings, R. A. Shields and H. J. Testa.
Imaging diseased bowel with indium-111 labelled white cells, by S. Saverymuttu, A. M. Peters, V. S. Chadwick, H. J. Hodgson and J. P. Lavender.

ASSESSING SMALL INTESTINAL FUNCTION

By I. W. Percy-Robb

Royal Infirmary, Edinburgh

This contribution consisted of a review of current approaches to the investigation of patients with suspected intestinal malabsorption and included methods for the assessment of intestinal absorption of dietary carbohydrate and fat. Physiological aspects of the entero-hepatic circulation of bile salts and methods currently in use for their investigation were also reviewed.

RADIOISOTOPES IN TESTING ILEAL FUNCTION

By M. van Blankenstein, J. W. O. v. d. Berg, R. de Groot and H. Delhez

Department of Medicine II, Erasmus University, Rotterdam and Rotterdam Radiotherapeutic Institute, Netherlands

The ileum has two specific functions, the absorption of vitamin B_{12} and of conjugated bile acids. The latter function can be investigated by the (1–^{14}C) glycocholate breath-test (GCA breath-test) and oral (24–^{14}C) taurocholate faecal-excretion test (TCA T/2).

The GCA breath-test measures the bacterial deconjugation of ^{14}C glycine from cholate. The ^{14}C glycine is subsequently converted to $^{14}CO_2$ and exhaled. In the test 185 kBq (5 μCi) of ^{14}C glycocholate is given in a Lundh meal and patients exhale hourly into a fixed amount of phenethylamine during 8 h. Bacterial deconjugation of glycocholate can result from bile acid malabsorption in the ileum, resulting in an overspill into bacteria-rich colon or from bacterial overgrowth of the small bowel. In bacterial overgrowth the peak value tends to occur within 4 h of the start of the test, while ileal malabsorption gives a peak later than 4 h. A more specific investigation for ileal bile-acid malabsorption is the TCA T/2 test. 185 kBq of (24–^{14}C) taurocholic acid is given in a Lundh meal and stools are collected in 24 h periods for five days. A 1 ml sample from each 24 h stool collection is burned in oxygen, the CO_2 collected in phenethylamine and the radioactivity measured. The results are expressed as a T/2.

Normal volunteers and patients with non-ileal diarrhoea have a T/2 of three days or longer. In practically all patients with ileal disease (Crohn's disease, resections and pelvic radiotherapy) the T/2 was under 2.5 days. An abnormally short T/2 with a normal ileum can be found in hormone-induced secretory diarrhoea and in post-vagotomy states. The use of ^{75}SeHCAT promises to simplify this test, as the whole 24-h stool collection can be measured without sampling. The use of this agent will enable any hospital with facilities for γ counting to employ this sophisticated test for the intactness of the entero-hepatic bile-acid circulation.

DYNAMIC IMAGING OF THE ENTEROHEPATIC CIRCULATION WITH SeHCAT

By S. T. Meller, R. M. Kupfer, R. P. Jazwari, J. H. Payne, V. R. McCready and T. C. Northfield

Departments of Nuclear Medicine and Physics, Royal Marsden Hospital, and Department of Medicine, St. George's Hospital Medical School, London

A ^{75}Se-labelled bile acid (SeHCAT SCQ3415, Radiochemical Centre, Amersham) has been used in five healthy volunteers to study the dynamics of the enterohepatic circulation of bile acids. The study was recorded on two successive days using a gamma camera/computer system. 900 kBq (25 μCi) SeHCAT was taken orally on the first day with a standard meal, and bile-acid recycling time was determined from the first appearance of SeHCAT in the liver and gall bladder. The small intestinal transit time was simultaneously measured by the hydrogen breath-test for comparison. On the second day the fasting distribution of SeHCAT was determined by static abdominal scintigrams. Gall-bladder contraction was then stimulated and a 2–3 h dynamic study recorded to study recirculation. In some subjects comparative data for gall-bladder emptying of a non-absorbable bile analogue (^{99}Tc^{m}–HIDA) were available.

---

*No reprints of these proceedings are available.

The SeHCAT curve was identical for the emptying phase, but then rose again. The difference between the two curves indicated gall-bladder refilling, and the point of divergence the bile-acid recycling time which agreed closely with the independent measurement obtained on the first day. Bile acid recycling time varied between 45 and 100 min (mean 62 min), compared with 160–265 min (mean 195 min) for small intestinal transit time. The distribution of the bile-acid pool was also determined. When fasting, 34–68% (mean 52%) was in the gall-bladder, but this fell to a minimum of 9–26% (mean 17%) during eating. We conclude that dynamic imaging with SeHCAT is a valuable non-invasive method for the study of the enterohepatic circulation in health and disease.

THE DETECTION OF ILEAL DISEASE WITH SeHCAT

By H. Nylhin

University of Umea, Sweden,

M. A. Eastwood and M. V. Merrick

Western General Hospital, Edinburgh

The major site of absorption of conjugated bile acids is considered to be the distal ileum. Measurement of their absorption gives an indication of ileal dysfunction. This is now possible, using a selenium-tagged bile acid—SeHCAT.

The aim of this study has been to evaluate SeHCAT as a measure of ileal function in patients with documented disease of the ileum and colon. After administration of 37 kBq (1 μCi) SeHCAT orally the whole-body retention of SeHCAT was measured on three occasions using a shadow-shield whole-body counter at 0, 4 and 7 days. Our controls were 20 persons free of gastro-intestinal disease. The study comprised 15 patients with Crohn's disease, two with jejuno-ileal bypass operations, 11 with ulcerative colitis and five with ileostomy following colectomy for severe colitis.

At 14 days a whole-body retention of less than 35% was regarded as abnormal. The patients with Crohn's disease confined to the ileum were below normal, as were the patients with jejuno-ileal bypass operations. The ileostomy patients also showed a reduced retention. At seven days a whole-body retention of less than 12% is definitely abnormal, and below 17% probably abnormal. All but one of the patients with ulcerative colitis were within normal limits.

Only one of the patients with small-intestinal Crohn's had a normal SeHCAT retention, and this patient also had a normal Schilling test and normal faecal bile-acid excretion. The figures for two other patients fell between 12% and 17%, and for all the others were below 12%. As a whole, the whole-body retention in patients with small-intestinal and ileocaecal disease was significantly reduced both at four and seven days using Wilcoxon's Rank Sum Test at $p < 0.001$.

As a conclusion, SeHCAT appears to hold promise as an easy and acceptable method to study ileal function. This study has to be regarded as a first view or introductory. We think that the SeHCAT warrants interest and further examination.

DETECTION OF ILEAL DYSFUNCTION USING SeHCAT

By Elizabeth A. Fagan, I. M. Baird and V. S. Chadwick

Departments of Medicine, West Middlesex University Hospital, and Royal Postgraduate Medical School, London

Whole-body retention of the γ-emitting radioisotopic bile-salt analogue SeHCAT (taurine conjugate of 23(^{75}Se)-25-homocholic acid) after oral administration has been proposed as a discriminant test of ileal dysfunction. This test has been evaluated in ten normal volunteers, 17 patients with Crohn's disease (ten with previous resection) and three patients with ulcerative colitis. ^{14}C-cholyl-*l*-glycine breath tests (six hour cumulative $^{14}CO_2$ excretion) and measurements of vitamin B_{12} absorption (standard Schilling test and whole-body counting technique) were performed in the same patients.

Whole-body retention of SeHCAT (410 kBq (11 μCi) dose) at 168 h was greater than 5% (range 6–59%) in all normal volunteers and all the six patients with disease confined to the colon (three Crohn's, three ulcerative colitis). The remaining 14 patients retained less than 5% (range 0–4%), and all had disease and/or resection of the ileum.

SeHCAT retentions at 0, 6, 12, 24, 48, and 96 h and daily faecal excretion were also measured. Retention at 96 h and faecal excretion over the first 48 h proved the most discriminant of these; however, there were three and nine of the patients respectively with normal results in the ileal disease group (false negatives). Patients with colonic disease showed sub-normal faecal excretion of SeHCAT. A comparison between SeHCAT and the other function tests is shown below.

Ileal disease	SeHCAT retention		SeHCAT excretion	^{14}C cholyl glycine breath test	Vitamin B_{12} Schilling retention	
	96 h	168 h	48 h	6 h	24 h	7 days
False positive	0	0	0	0	0	3
False negative	3	0	9	10	2	5

Whole-body retention of SeHCAT at 168 h accurately detected the presence or absence of ileal disease or resection in 20 patients with inflammatory bowel disease. Good discrimination was also found with the standard Schilling test. Variations on the SeHCAT test were less discriminant. Faecal excretion of SeHCAT was sub-normal in patients with active colonic inflammation.

HEPATIC CLEARANCE OF A RADIOLABELLED BILE ACID AS A TEST OF LIVER FUNCTION

By J. H. Marigold

St. Thomas' Hospital, London

Conventional liver-function tests, such as alkaline phosphatase and the aminotransferases, are not necessarily tests of liver-cell function, but merely reflect enzyme leakage from damaged hepatocytes. Measurement of the hepatic removal of bile acids from blood is theoretically a sensitive test of liver function, since bile acids are endogenous organic anions that are rapidly and exclusively removed by the liver, unlike the exogenous dyes (bromosulphthalien and indocyanine green) that have been used previously. Interest in bile acids for testing liver function was stimulated by the development of methods permitting accurate measurement of their concentration in blood. An intravenous glycocholic acid mass-loading test was soon replaced by a test using a tracer dose of ^{14}C-glycocholic acid. Although the initial results were promising, several reports have now confirmed that measurement of the intravenous clearance of ^{14}C-glycocholic acid is not able to detect mild liver disease better than conventional liver function tests. This is because clearance after intravenous administration of a substance with a high hepatic extraction ratio is much more dependent on liver blood flow than on liver-cell function.

When given orally, however, all of the bile acid has to pass through the liver before reaching the systemic circulation, and clearance is then more dependent on liver-cell function than on liver blood flow. Simultaneous tracer doses of ^{14}C- and ^{3}H-labelled cholic acid have been given intravenously and orally, and the results have confirmed that the oral clearance is more sensitive to changes in liver function than the intravenous clearance. Other studies using mass doses of cholic acid or ursodeoxycholic acid have suggested these are sensitive tests. A study using ^{14}C-labelled tracer and mass dose of chenodeoxycholic acid is in progress: addition of a mass dose to the tracer stresses the hepatic uptake mechanism, and this test should therefore be more sensitive than when the tracer dose is given alone.

GASTRIC EMPTYING REVISITED

By L. K. Harding

Dudley Road Hospital, Birmingham

Radioisotopic methods are preferable to aspiration or radiological techniques for measuring gastric emptying because they are not unpleasant for the patient, can be quantified continuously and provide a measure of the volume of meal in the stomach rather than the combined volume of meal and secretions. The position of the patient is important since emptying is gravity-dependent, especially after surgery. In order to examine early gastric emptying it is essential to determine the volume remaining in the stomach at each time interval, and this can be assessed by relating the peak count in the whole field of view to that in the stomach. Aspiration experiments confirm this assessment. Either a logarithmic or a linear description of the later phase of emptying is appropriate but care must be taken not to include data in the analysis from when the stomach is almost empty. It is suggested that the emptying study should be discontinued when the volume in the stomach reaches half its peak value.

A variety of radiopharmaceuticals has been used for gastric emptying but ^{113}In^{m} has the advantage of a high γ energy, short half-life, minimal adsorption onto the gastric mucosa and minimal absorption. The best type of meal to use depends on the purpose of the examination. The symptom of dumping is related to rapid early emptying of a liquid meal, whereas gastric stasis is associated with delayed emptying of a solid meal.

There are three main sources of error in gastric emptying studies and these are additive. Scatter and septal penetration result in counts from the stomach being detected outside the stomach area. A 16% underestimate of the peak volume occurs with an average stomach and the error is inversely proportional to stomach size. Movement forward of the stomach during the study causes an underestimate in emptying rate between 8% and 26% but less with higher energy γ rays. Finally, bowel overlap is significant in patients with large stomachs, notably those with gastric ulcer, and in these circumstances the technique is inapplicable.

GASTRIC EMPTYING OF SOLIDS

By R. C. Heading, S. Holt, J. Reid, T. V. Taylor and P. Tothill

Departments of Therapeutics, Clinical Surgery and Medical Physics, Royal Infirmary of Edinburgh

Although the basic techniques of scintigraphic measurement of gastric emptying are now well established, various radionuclide-labelled solid meals have been developed, each being promoted as an optimum indicator of "physiological" gastric emptying. We have undertaken a direct comparison of gastric emptying of a digestible solid (^{113}In^{m} labelled chicken liver) and of small inert particles (^{99}Tc^{m} labelled paper squares) incorporated in a mixed solid–liquid meal to investigate the importance of the character of the solid in determining its emptying rate and pattern.

On two occasions, six normal subjects were given the meal containing the labelled liver and the inert particles. On one occasion the liver was given as 1 cm cubes, on the other occasion as 0.3 cm cubes. Gastric emptying rates of the liver and of the particles were measured simultaneously by sequential scintiscanning. Subsequently, similar measurements using 1 cm liver cubes were carried out on five patients who had previously undergone gastric surgery.

In the normal subjects, initial emptying of the liver was slower than that of the inert particles ($p < 0.05$) for both sizes of liver cubes. Liver emptying then accelerated to be faster than the particles ($p < 0.05$). Overall emptying of the liver given as small cubes was faster than large cubes, times to 50% emptying being 50 min and 70 min respectively. In the post-operative subjects, emptying of the liver and of the inert particles was identical.

The differences in emptying of the two types of solid in normal subjects are consistent with the view that solid food such as liver is ground down and "liquefied" in the stomach prior to emptying. The size of ingested food particles apparently influences the rate of liquefaction and thus of emptying. However, although different emptying patterns are apparent, the fundamental difference in nature of the two types of solid has surprisingly little effect on the overall rates at which they are emptied from the stomach.

INTERPRETATION OF GASTRIC EMPTYING IN PATIENTS WITH DYSPEPSIA

By S. L. Grainger, Judith I. Gaunt, R. P. H. Thompson and D. N. Croft

Gastrointestinal Laboratory and Department of Nuclear Medicine, St. Thomas' Hospital, London

Gastric emptying of radiolabelled solid, measured with an anteriorly placed gamma camera, does not appear to start for up to 2 h following a meal in some patients. Using ^{99}Tc^{m} poached egg-white as solid-phase marker, we have found that delayed emptying also occurs in patients with dyspepsia, but this might be due to an artefact arising from PA movement of gastric food. Alternatively it might be due to a real delay in emptying of solid from the stomach as a result, for example, of poor antral grinding.

Linear regression analysis against time of the counts recorded for one hour within the region of interest (ROI) outlining the stomach gave a horizontal line. If only the counts from 30–60 min were analysed, the emptying rates determined from the regression coefficients were similar to those studies where the effect of food movement was eliminated by double-headed counters. This method of analysis suggests an initial lag phase during which solid food fails to empty from the stomach.

A "lag time" was therefore calculated as the time at which the line describing the terminal phase, when extrapolated backwards, reached the level of the maximum counts in the ROI. The emptying rate from the slope of the terminal phase did not differ in eight control subjects or seven patients with dyspepsia; however, the lag time was significantly prolonged in the patients ($p < 0.05$, Wilcoxon rank sum test). This study reveals abnormal gastric function in patients with dyspepsia.

GASTRIC MUCOSAL UPTAKE OF PERTECHNETATE—CONTROVERSY AND CLINICAL APPLICATIONS

By J. G. Williams

Royal Naval Hospital, Plymouth

Technetium-99m pertechnetate is known to concentrate in the stomach following intravenous injection, but there is controversy as to the cellular site of this uptake. Evidence for the parietal cell comes from an auto-radiographic study in cats and man (Meier-Ruge and Fridrich, 1969) and from the observation that gastric concentration of pertechnetate, as measured by aspiration or by external counting, correlates well with acid output when the stomach is stimulated by histamine (Wine *et al.*, 1976), or pentagastrin (Taylor *et al.*, 1975). Evidence that the gastric mucus-secreting epithelial cell may be responsible comes from auto-radiographic studies in many different animals (Bartelink *et al.*, 1966; Berquist *et al.*, 1976; Chaudhuri, 1975, 1976; Priebe *et al.*, 1974) and from the observation that the unstimulated achlorhydric stomach in pernicious anaemia concentrates pertechnetate with an avidity similar to that seen in normals (Chaudhuri, 1977). Animal studies have shown that antral tissue devoid of parietal cells concentrates the isotope (Safaie-Shirazi *et al.*, 1973, Keramidas *et al.*, 1974; Chaudhuri *et al.*, 1973). Finally, it has been shown that, in patients with peptic ulcer, gastric mucosal uptake of intravenous pertechnetate is increased by carbonoxolone but unaffected by cimetidine (Williams and Croft, 1980). On the evidence available it seems most likely that uptake occurs primarily in the mucous epithelial cells of the stomach, but that this is related to blood flow, the health of mucosal cells and the surface area of the stomach.

Quantification of uptake using a single-scan technique has been used to estimate acid output (Taylor *et al.*, 1979). Other clinical applications include the detection of ectopic gastric mucosa. This applies to conditions such as Barrett's oesophagus (Sailer and Janeway, 1978), retained gastric antrum (Chaudhuri *et al.*, 1973; Sciarretta *et al.*, 1978), gastrogenic cyst (Mark *et al.*, 1973), intestinal duplication (Barkley *et al.*, 1977) and Meckel's diverticulum (Berquist *et al.*, 1976; Gelfand *et al.*, 1978). In atrophic gastritis the stomach can be visualized, though uptake tends to be patchy in the presence of intestinal metaplasia (Bartelink *et al.*, 1966). This may have clinical application in screening for pre-malignancy.

REFERENCES

BARKLEY, R. M., MUNOZ, O. and PARKEY, R. W., 1977. Intestinal duplication detected with technetium-99m sodium pertechnetate imaging of the abdomen. *Digestive Diseases*, *22*, 1122–1126.

BARTELINK, A., SMEETS, E. H. J., HOEDEMAKER, PH. J., VEEGER, W., WORLDRING, M. G. and ABELS, J., 1966. 99m Tc in the examination of the stomach. In *Proceedings IX International Congress of Internal Medicine* (ed. A. J. Dunning) (Excerpta Medica, Amsterdam), pp. 381–387.

BERQUIST, T. H., NOLAN, N. G., STEPHENS, D. H. and CALSON, H. C., 1976. Specificity of 99m Tc pertechnetate in scintigraphic diagnosis of Meckle's diverticulum; review of 100 cases. *Journal of Nuclear Medicine*, *17*, 465–469.

CHAUDHURI, T. K., 1975. Cellular site of secretion of 99m TcO_4 in the stomach—a controversial point. *Journal of Nuclear Medicine 16*, 1204–1205.

1976. Cellular site of secretion of 99m TcO_4 in the stomach—a controversial point. *Journal of Nuclear Medicine*, *17*, 756–757.

1977. Can 99m Tc pertechnetate be used to assess the secretion of gastric acid in pericious anaemia. *Journal of Nuclear Medicine*, *18*, 121–122.

CHAUDHURI, T. K., CHAUDHURI, T. K., SHIRAZI, S. and CONDON, R. E., 1973. Radioisotope scan—a possible aid in differentiating retained gastric antrum from Zollinger-Ellison syndrome in patients with a recurrent peptic ulcer. *Gastroenterology*, *65*, 697–698.

GELFAND, M. J., SILBERSTEIN, E. B. and COX, J., 1978. Radionuclide imaging of Meckel's diverticulum in children. *Clinical Nuclear Medicine*, *3*, 4–8.

KERAMIDAS, D. C., CORAN, A. G. and ZALESKA, R. W., 1974. *Journal of Paediatric Surgery*, *9*, 879–883.

MARK, R., YOUNG, L., FERGUSON, C. and SUTHERLAND, J. B., 1973. Diagnosis of intrathoracic gastrogenic cyst using 99m Tc pertechnetate. *Radiology*, *109*, 137–138.

MEIER-RUGE, W. and FRIDRICH, R., 1969. Die Verteilung von Technetium-99m und Jod-131 in der Magenschleimhaut. *Histochemie*, *19*, 147–154.

PRIEBE, C. J., JR., MARSDEN, D. S. and LAZAREVIC, B., 1974. The use of 99m technetium pertechnetate to detect transplanted gastric mucosa in the dog. *Journal of Paediatric Surgery 9*, 605–613.

SAFAIE-SHIRAZI, S., CHAUDHURI, T. K., CHAUDHURI, T. K., and CONDON, R. E., 1973. Visualization of isolated retained antrum by using technetium 99m. *Surgery*, *73*, 278–283.

SAILER, J. F. and JANEWAY, C. M. J., 1978. Pertechnetate demonstration of a Barretts oesophagus involving the length of the oesophagus. *Journal of Nuclear Medicine*, *19*, 1366–1368.

SCIARRETTA, G., MALAGUTI, P., TURBA, E., FINI, A., VERRI, A., GARAGNANI, B. and CACCIARI, C., 1978. Retained gastric antrum syndrome diagnosed by 99m Tc pertechnetate scintiphotography in man; hormonal and radioisotopic study of 2 cases. *Journal of Nuclear Medicine*, *19*, 377–380.

TAYLOR, T. V., PULLAN, B. R., ELDER, J. B. and TORRANCE, B., 1975. Observations of gastric mucosal blood flow using 99 Tcm in rat and man. *British Journal of Surgery*, *62*, 788–791.

TAYLOR, T. V., HOLT, C., MCLOUGHLIN, G. P. and HEADING, R. C., 1979. A single scan technique for estimating acid output. *Gastroenterology*, 77, 1241–1244.

WILLIAMS, J. G. and CROFT, D. N., 1980. Carbonoxolone and gastric technetium-99m pertechnetate uptake in patients with gastric ulceration. *Scandinavian Journal of Gastroenterology*, *15*, *Supplement 65*, 29–33.

WINE, C. R., NAHROWOLD, D. L., ROSE, R. C. and MILLER, K. L., 1976. Effect of histamine on technetium 99m excretion by gastric mucosa. *Surgery*, *80*, 591–594.

RADIOISOTOPE MILK SCANS IN PAEDIATRICS

By I. Gordon

Department of Paediatric Radiology, Hospital for Sick Children, Great Ormond Street, London WC1

Gastro-oesophageal reflux constitutes a potentially serious disease in paediatrics. It is an important cause of vomiting and failure to thrive in infancy; when associated with aspiration it may be the cause of recurrent chest infections.

The barium swallow has been the major investigation but monitoring the oesophageal pH (Tuttle test) and lower oesophageal pressure have also been carried out. All these investigations have certain drawbacks.

Orange juice/milk has been labelled with $^{99}\mathrm{Tc}^{\mathrm{m}}$ sulphur colloid (185 kBq/ml). After ingestion of 100–200 ml of milk or orange juice the child lies supine over the camera face for one hour. Delayed images at 4 and 24 h are also obtained. All the data are accumulated onto an on-line computer (1 min per frame). The results are given in the table.

		Milk scan	
		Positive	Negative
Barium study	Positive	15	10
	Negative	5	7

These results are in keeping with other published data. In the scan-positive patients there were four in whom aspiration into the lung was observed in addition to the gastro-oesophageal reflux, two with positive barium results and two with negative results. In all the barium positive cases only gastro-oesophageal reflux was detected, no secondary pulmonary aspiration being documented. There were five patients with a positive milk scan and a negative barium examination and ten patients with a negative milk scan and a positive barium examination.

In children with clinical suspicion of gastro-oesophageal reflux, a barium meal is the first imaging investigation. If positive, no further steps are necessary. If negative, then a milk scan is the next investigation. When recurrent chest infection is being investigated, a milk scan is the only positive way of demonstrating aspiration from secondary gastro-oesophageal reflux.

RADIONUCLIDE TRANSIT STUDIES OF THE OESOPHAGUS

By J. N. Blackwell, R. C. Heading, S. Holt, W. J. Hannan and P. Tothill

Departments of Therapeutics and Medical Physics, Royal Infirmary, Edinburgh

Current methods of investigating patients with motility disorders of the oesophagus are unsatisfactory. Contrast radiography is insensitive and manometry is both time-consuming and uncomfortable for the patient. Our aim was to assess whether oesophageal radionuclide transit studies might prove a satisfactorily sensitive, objective and non-invasive method for identifying oesophageal dysfunction.

Sixteen normal volunteers (aged 19–87 years) were studied to ascertain the normal range and reproducibility of transit times. A bolus of 20 MBq (500 μCi) of $^{99}\mathrm{Tc}^{\mathrm{m}}$ sulphur colloid in 10 ml of water was swallowed, with the patient positioned supine beneath a gamma camera linked to video recorder. Computer processing allowed analysis of time-activity curves for the upper, middle and lower thirds of the oesophagus. The average mean transit time in the normal subjects was 2.5 s ($\pm$SD 0.9), with a range of 0.9 to 4.5 s. The average total transit time was 7.3 s ($\pm$SD 2.3) with a range of 5.0 to 13.0 s. The transit times were found to be highly reproducible in the nine normal subjects who underwent a second study.

The procedure was then undertaken twice on eight patients with diffuse oesophageal spasm, one with achalasia, one with scleroderma and one with non-specific dysmotility. Oesophageal dysmotility had been confirmed in all cases by manometry, being continuous in nine patients and intermittent in two. The total nuclide transit time (which proved the more useful measurement) was markedly prolonged in the nine patients who had persistent manometric abnormalities and covered a range from 20 to more than 120 s. In the two patients with intermittent dysmotility the total transit times were 9 and 13 s.

Radionuclide transit measurement is a quick, comfortable and reproducible new procedure which should prove useful in identifying oesophageal disorders.

OBSERVATIONS OF $^{14}\mathrm{CO}_2$ BREATH EXCRETION PATTERNS USING AN ORALLY ADMINISTERED PREPARATION OF $^{14}\mathrm{C}$-LABELLED CELLULOSE

By J. M. Findlay, G. C. Hart, T. Srinivasan, B. Selby and K. M. Davis

Department of Medical Physics, Duckworth Lane, Bradford, West Yorkshire BD9 6RJ

The hypothesis was examined that if man was fed a $^{14}\mathrm{C}$-labelled cellulose preparation, $^{14}\mathrm{CO}_2$ might be observed in expired air, indicating the possibility of cellulose metabolism in the GI tract. $^{14}\mathrm{C}$-cellulose (ICN Pharmaceuticals) was prepared by photosynthesizing *Canna indica* leaves in an atmosphere of $^{14}\mathrm{CO}_2$ for 24 hours, other organic fractions being removed subsequently by a series of washings.

Three groups of patients were studied: 12 controls; six patients with colonic cancer before and after sterilization of the bowel and a low-residue regimen; and six ileostomy subjects. After fasting overnight the $^{14}\mathrm{C}$-cellulose was administered and duplicate breath samples obtained over a period of 24 hours.

Activity-time curves were drawn and the area under these curves was quantitated over four time-spans: 0–4 h, 4–8 h, 8–14 h and 14–22 h. Whilst there is a wide variation in the amount of $^{14}\mathrm{CO}_2$ expired within the control and pre-colon-sterilization groups, the amounts in the two groups are not significantly different. Patterns of response can be seen, and the amount of $^{14}\mathrm{CO}_2$ expired is significantly ($p < 0.01$) reduced in both the post-colon-sterilization and ileostomy groups. The data suggest that the preparation is metabolized both in the small and large bowel, but the amount recovered, although comparable with that from other established breath tests, is low and labelled impurities could account for some or all of the observations.

THE FORMATION OF FUNCTIONAL IMAGES FROM THE HIDA SCAN

By D. L. Hastings, R. W. Nicholson, R. A. Shields and H. J. Testa

Departments of Medical Physics and Nuclear Medicine, Manchester Royal Infirmary, Oxford Road, Manchester

$^{99}\mathrm{Tc}^{\mathrm{m}}$-labelled HIDA (H-diethyl-IDA) is a hepatobiliary imaging agent which follows the same pathway as bile through the liver and biliary system. Gamma-camera images for a normal subject demonstrate the liver, bile ducts, gall bladder and intestine. If the gamma camera is on-line to a computer acquisition and storage system, further information may be obtained by generating activity-time curves for selected regions.

In this presentation a new technique is described for presenting the HIDA images. On the computer one-minute images were acquired for one hour, and from these, six images were produced by summing three images at ten-minute intervals. A sequence of five different images was then derived by subtracting each summed image from the next. In order to eliminate negative numbers a large positive constant (10000) was added to each resulting pixel. Pixels greater than the constant represented accumulation of HIDA during the interval between the two summed images, and pixels less than the constant represented elimination.

The method for displaying the functional images is as important as the method of generation. Pixels greater than the constant are displayed in red and those less than the constant in green. The colour ramp has a total of 16 levels, and is black at the centre incrementing to full red in level 16 and to full green in level one. Thus the brighter the red the greater the accumulation of HIDA, and the brighter the green the greater the elimination.

The functional images for a normal subject show accumulation in the liver and biliary tree in the first image and the subsequent ones clearly show elimination from the liver parenchyma, accumulation followed by elimination in the gall bladder and common bile duct, and movement through the intestine.

These types of functional images are a coarse form of differentiation of the dynamic scan with respect to time. The information contained in them is the rate at which HIDA is being treated in different regions of the liver and bile ducts.

CLINICAL APPLICATIONS OF FUNCTIONAL IMAGES FROM THE HIDA SCAN

By R. W. Nicholson, D. L. Hastings, R. A. Shields and H. J. Testa

Departments of Medical Physics and Nuclear Medicine, Manchester Royal Infirmary, Oxford Road, Manchester

Functional images were generated from a series of HIDA scans as described in the previous paper. The results from 35 scans were analysed to determine the clinical value of the technique of functional imaging, with particular reference to two specific situations. Firstly, differentiation between obstructive jaundice and hepatocellular disease, and secondly determination of the significance of the persistence of activity in the biliary tree on the analogue pictures.

In general, little additional information is obtained from functional images over the analogue images, but it is, in certain respects, in a more easily readable form.

In normal subjects there is usually a rapid uptake and prompt excretion of HIDA and often a transiently seen biliary tree which both fills and empties rapidly. In patients with epahtocellular disease, excretion may be slow and delayed, but is uniform over the liver as a whole. Patients with biliary obstructive disease tend to show a persistently filling biliary tree, but this is dependent on a reduced rather than totally absent flow of bile down the biliary tree. Thus, if no activity is seen to appear in any of gut, gall bladder or bile ducts, a total biliary obstruction cannot be excluded, and in such cases the technique remains incapable of accurately distinguishing between the two causes of jaundice.

For this and other reasons, the HIDA scan must remain one of a "team" of investigations available to the clinician.

IMAGING DISEASED BOWEL WITH INDIUM-111 LABELLED WHITE CELLS

By S. Saverymuttu, A. M. Peters, V. S. Chadwick, H. J. Hodgson and J. P. Lavender

Hammersmith Hospital, London W12 0HS

The potential value of ^{111}In-labelled autologous white cells in localizing diseased bowel was studied in 40 patients with a variety of bowel disorders. White cells were separated from whole blood by first allowing the red cells to sediment at 1 g for 30–45 min and then centrifuging the leucocyte and platelet-rich plasma at 100 g for 10 min. The cells, resuspended in dextrose saline, were labelled with ^{111}In-acetylacetone in 20 mM Hepes buffer. Scans were performed at 3 h or 4 h and 24 h after reinjection of the white cells. Stools were collected for four days and the total ^{111}In content measured to determine the percentage of the administered dose excreted.

The scans in control patients with the irritable-bowel syndrome showed the expected visualization of the liver, spleen and bone marrow and no other intra-abdominal localization. In the patients with Crohn's disease, early scans showed localization at the site of intestinal involvement. Later scans demonstrated a column of activity in transit in the bowel lumen distal to the site of initial localization. Faecal counting showed a mean recovery of 8% with a range of 2–34%, the most strongly positive scan producing the greatest faecal recovery. Two patients with radiation enteritis showed a similar series of positive scans; one in whom faecal quantitation was performed excreted 13% of the dose. A patient with graft versus host disease with bowel involvement had a positive scan with 8% excretion. All the irritable-bowel syndrome patients had negative scans with a mean excretion of 0.4% (range 0–1%).

^{111}In-labelled white-cell scanning, which is non-invasive and requires no preparation of the patient, is useful in localizing diseased bowel and may prove to be an aid in assessing disease activity.

Combined radiotherapy and chemotherapy: advantages, disadvantages—can radiobiology help?

Abstracts of papers presented at a meeting held at The British Institute of Radiology, 32 Welbeck Street, W1M 7PG on Thursday, February 19, 1981

Chairman: Dr. Dorothy Pearson

The historical background of radiotherapy and chemotherapy in childhood cancers, by Dorothy Pearson.
The advantages of combined radiotherapy and chemotherapy in childhood cancer, by M. Ruth Sandland.
The problems of combined radiotherapy and chemotherapy in childhood cancer, by D. P. Deakin.
Experimental combinations of cytotoxic drugs and radiation, by J. V. Moore.

THE HISTORICAL BACKGROUND OF RADIOTHERAPY AND CHEMOTHERAPY IN CHILDHOOD CANCERS

By Dorothy Pearson

Christie Hospital and Holt Radium Institute, Manchester M20 9BX

The development of the treatment of children with cancer has taken place over a very short time. Before 1940 only those tumours amenable to surgery could be treated. From that time radiotherapy came to be used in an increasing amount, and by the beginning of the next decade some tumours were being successfully treated by both surgery and radiotherapy or a combination of the two.

Our knowledge, however, of the extent of childhood malignancy was unknown, so in 1953 the Manchester Children's Tumour Registry was set up to find out both the incidence of children's tumours and also how well the children were treated.

A study of the first ten years of the registry showed that there were 105 cases of malignant disease in childhood in the NW Region of England, in which the population of children under 15 years of age is one million. This survey also showed the many different tumours which occurred, and the success with the then available treatments. Apart from one or two exceptions such as retinoblastoma the cure rate for most was poor, rarely exceeding 30%, and zero in such diseases as leukaemia.

With this background, when cytotoxic drugs were discovered it seemed natural to try them in these patients. Drugs have been used in the treatment of malignant disease since the last century, but it was not until 1943 that the first effective agent—nitrogen mustard—was produced. By 1948 patients with leukaemia could be induced into a remission with a folic acid antagonist. Since then other drugs have followed—used at first for relapsed patients and then later as adjuvant treatment with surgery and radiotherapy. In all more than thirty drugs have been used in the paediatric field alone. These changes have led to improvements in survival but also problems, as radiotherapy and chemotherapy have to learn to live together to the best advantage.

THE ADVANTAGES OF COMBINED RADIOTHERAPY AND CHEMOTHERAPY IN CHILDHOOD CANCER

By M. Ruth Sandland

Department of Radiotherapy,
St. Bartholomew's Hospital, and Hospital for Sick Children,
Great Ormond Street, London

The ability of chemotherapy to control metastatic disease in many childhood tumours has led to a re-evaluation of the role of different modalities in the ablation of the primary tumour.

While surgical removal of the primary remains important in the treatment of certain tumours such as nephroblastoma, it is now possible in others, including rhabdomyosarcomata of the orbit and pelvic viscera, to avoid radical surgery with its consequent disability or deformity and rely rather on irradiation and chemotherapy. The current approach to these tumours is detailed.

The use of more intensive chemotherapy regimes before initiating irradiation of the primary lesion makes it possible to consider smaller treatment volumes and even lower total doses without prejudicing local control rates. Indeed, in nephroblastoma, post-nephrectomy irradiation has been discarded in stage I cases, and in later stage cases with an increased risk of local relapse the dose used is lower than formerly. However, data on this point for some other tumours are conflicting, especially when the amount of bone irradiated and the dose employed are studied in Ewing's sarcoma.

By painstaking collaborative studies in special centres, so ably pioneered in this field in the USA, it is expected that combined treatment regimes of greater efficacy but with decreased undesirable short-term or long-term consequences will be devised.

REFERENCES

D'ANGIO, G., 1980. Wilms' tumour: an update. *Cancer*, *45*, 1791–1798.

RAZEK, A., PEREZ, C. A., TEFFT, M., NESBIT, M., VIETTI, T., BURGERT, E. O., KISSANE, J., PRITCHARD, D. J., and GEHAN, E. A., 1980. Intergroup Ewing's sarcoma study. Local control related to radiation dose, volume and site of primary lesion in Ewing's sarcoma. *Cancer*, *46*, 516–521.

THE PROBLEMS OF COMBINED RADIOTHERAPY AND CHEMOTHERAPY IN CHILDHOOD CANCER

By D. P. Deakin

Christie Hospital and Holt Radium Institute,
Manchester M20 9BX

A knowledge of the tolerance of normal tissues is the foundation upon which any radiotherapy dosage system is built. A body of clinical and experimental data has now grown up indicating that normal-tissue reactions to radiation are altered—often increased—by concurrent drug administration. In Manchester, acute radiation toxicity has been seen when radiotherapy has been combined with actinomycin-D for the treatment of nephroblastoma in childhood, for example:

Moist skin desquamation and confluent mucosal fibrin at 1200 cGy in four days;

Acute liver necrosis at 3000 cGy in four weeks;

Acute pneumonitis at 2000 cGy in three weeks;

Acute renal failure at 2000 cGy in three weeks and at 1500 cGy in three weeks.

It is now clear that actinomycin-D and adriamycin should not be given during the course of a radiotherapy treatment. Even when these drugs are given later a settling radiation reaction may be re-induced. Severe acute reactions may settle but lead to later impairment of structure and function of an organ. Some specific late effects are seen with combinations of radiotherapy and chemotherapy, however. Study of children treated in Manchester on various protocols for acute lymphoblastic leukaemia reveals cerebral calcification in 35%. The incidence varies with the different protocols but is highest when cranial irradiation and intravenous methotrexate are combined. Second malignancies are seen in some children cured of cancer by surgery or radiotherapy and the incidence of these may be increased by the addition of chemotherapy. Careful, long-term follow-up and documentation are mandatory for all children treated for cancer.

EXPERIMENTAL COMBINATIONS OF CYTOTOXIC DRUGS AND RADIATION

By J. V. Moore

Paterson Laboratories,
Christie Hospital and Holt Radium Institute,
Manchester M20 9BX

There is now a large experimental literature on the combination of cytotoxic drugs and ionizing radiation. The great majority of studies have concentrated on (*a*) single doses of each agent, (*b*) experimentally accessible, *i.e.* rapidly renewing, normal tissues *e.g.* in gut, marrow and skin, and (*c*) intervals of a few hours between administration of modalities. For such intervals it has been possible to demonstrate (or infer) interactions between the effects of drugs and radiation in terms of altered capacity to accumulate or repair sublethal injury (ACT-D, ADR), synchronization of cells surviving a first treatment (VCR ?) or recruitment of resting cells into cycle (HU). Enhanced radiation effects resulting from these interactions can be minimized and even some "protection" achieved by adjusting the interval between modalities. Favourable and unfavourable intervals established for single doses may also apply for daily fractions, which we illustrate here by the response of the small intestine to VCR and γ rays. However, we also show that within this time scale of hours, optimal timing varies quite markedly between different combinations, even for drugs with ostensibly the same cell-cycle phase specificity.

The advantages to be gained in terms of normal-tissue sparing by increasing the interval between courses of agents to days or even weeks are discussed in terms of repopulation of cells and of phenomena such as "slow repair" in the lung (ADR). The constraint on this approach is the probability of regrowth of tumours which longer intervals might permit. Examples are cited of rapidly-growing rodent tumours for which longer intervals (ten days between CY and γ rays) were actually advantageous in terms of tumour oxygenation and it is also shown that cure rates are not necessarily prejudiced.

Radiobiology work-in-progress meeting

Abstract of papers presented at a meeting held on Friday, February 20, 1981 in the Reid-Knox Hall, 32 Welbeck Street, London W1M 7PG

Chairman: Professor R. J. Berry

Induction of resistance to X rays in *E. coli* by toluene, by N. E. Gillies and N. H. Ratnajothi.
A technique to predict and follow the biological effects of radiation and heat, by W. A. Cramp, J. Lunec, A. George, S. Cresswell, G. Harris and I. Olsen.
Relationship between cell-survival parameters—fact or artefact? by J. Kirk, G. F. Brunton and L. Wilson.
Relationship between cell-survival parameters—a biological interpretation, by G. F. Brunton and J. Kirk.
Interaction between X rays and neutrons, by N. J. McNally and J. de Ronde.
Linearity of induction of micronuclei at low doses in bean roots, by I. Diehl-Marshall and M. Bianchi.
The effect of dexamethasone on the radiation survival response and misonidazole-induced hypoxic-cell cytotoxicity in Chinese hamster cells V79–753B *in vitro*, by B. C. Millar and S. Jinks.
The enhancement of effect of chemotherapeutic agents by nitroimidazoles, by W. M. C. Martin and N. J. McNally.
A differential effect of misonidazole on the cytotoxicity of cyclophosphamide in tumour and normal tissues, by M. P. Law, D. G. Hirst and J. M. Brown.
Kinetics of response to irradiation of normal tissues with differing proliferative organisation, by T. E. Wheldon, J. Kirk and A. S. Michalowski.
The response of pig skin to non-uniform irradiation with beta-emitters of varying energy, by D. M. Peel and J. W. Hopewell.
Gastro-intestinal lesions in thorax-irradiated mice, by A. S. Michalowski.

INDUCTION OF RESISTANCE TO X RAYS IN *E. COLI* BY TOLUENE

By N. E. Gillies and N. H. Ratnajothi

Department of Biology as Applied to Medicine,
The Middlesex Hospital Medical School, London W1P 6DB

Treatment of *E. coli* K12 AB1157 with a low concentration of toluene (10 μM) in buffer for as short an interval as ten minutes induced a large shoulder in the X-ray survival curve. This effect was independent of the presence of oxygen at the time of irradiation. A small decrease in the final exponential slope of the survival curve was also observed, which is attributed to chemical protection effected by a small amount of toluene remaining after removal of the bulk of the chemical before irradiation. Although the mechanism of the effect is at present unknown, the alteration in the shape of the X-ray survival curve from exponential to sigmoid suggests that changes in the cell membranes to a more fluid configuration may occur. This would be expected if substantial removal of membrane proteins was caused by toluene, an effect known to occur after treatment with much higher concentrations of toluene (de Smet *et al.*, 1978). Thus, increased membrane fluidity may be the basis of the induction of the increased radiation resistance. Brief exposure to toluene did not cause genetically determined alterations in radiation sensitivity as evidenced by the finding that the shoulder in the survival curve was "lost" by applying one or other of two procedures to toluene-treated cells before they were irradiated. The first of these was incubation of the treated cells in nutrient broth at 37°C when the D_q of the X-ray survival curve was approximately halved for each doubling in cell number. This effect we have termed metabolic dilution. The second was storage of the treated cells in buffer at 4°C, when the shoulder of the X-ray survival curve gradually disappeared over a very much longer time interval than during the first procedure. The mechanism of the loss of shoulder caused by the second procedure appears to be different from that of the first and we have called this physicochemical decay.

REFERENCE

DE SMET, M. J., KINGMA, J. and WITHOLT, B., 1978. The effect of toluene on the structure and permeability of the outer and cytoplasmic membranes of *Escherichia coli*. *Biochimica et Biophysica Acta*, *506*, 64–80.

A TECHNIQUE TO PREDICT AND FOLLOW THE BIOLOGICAL EFFECTS OF RADIATION AND HEAT

By W. A. Cramp, J. Lunec, A. George and S. Cresswell

MRC Cyclotron Unit, Hammersmith Hospital,
Du Cane Road, London W12 0HS

and G. Harris and I. Olsen

Kennedy Institute, Bute Gardens, London W6

The nature of newly synthesized DNA in several mammalian cell lines has been investigated by hydroxylapatite chromatography before and after irradiation and heating. By observing the extent of bonding between newly synthesized DNA and parent DNA in unirradiated cells it is possible to predict the relative sensitivity of the cell lines to radiation. The bonding between the DNA strands, daughter and parent, decreases with time after irradiation, reaches a minimum and then returns to background levels. The extent of this phenomenon is dose dependent and is more pronounced in the presence of oxygen. The relative sensitivities of cell lines to heat cannot be so readily predicted from the normal background degree of strand bonding. There is however a close correlation between the lethal effect of heat and a decrease in post-heating strand bonding. The change with time of strand bonding after heat is markedly different to the response after radiation.

RELATIONSHIP BETWEEN CELL-SURVIVAL PARAMETERS—FACT OR ARTEFACT?

By J. Kirk, G. F. Brunton and L. Wilson*

Glasgow Radiobiology Group, Belvidere Hospital,
London Road, Glasgow G31 4PG
and
West of Scotland Health Boards,
Department of Clinical Physics and Bio-Engineering,
11 West Graham Street, Glasgow G4 9LF

A CHO cell line was serially sub-cultured to obtain a homogeneous cell line (SA12). That line was irradiated and a further eleven cell lines were derived from small clones of partially damaged cells at different times after irradiation. All cell lines which can be effectively classed as separate sub-lines on an equal basis were grown in Hams F12 medium, irradiated in plastic culture flasks with 250 kV X rays (HVL 2.5 mm Cu), and stained and cultured seven days later. Measured cell-survival fractions were in the range from 1 to 3.7×10^{-3}. The resulting cell-survival data demonstrated that curves with larger shoulders tended to have steeper terminal slopes and those with smaller shoulders smaller terminal slopes, indicating a possible relationship between cell-survival-curve parameters.

Using only fits significant at the 5% level, strong correlations between the parameters of these fits have been found for the following two-parameter cell-survival-curve formulations: multi-target ($p < 0.01$), quadratic ($p < 0.0001$), and Green-Burki ($p < 0.001$).

The possibility of this parametric relationship being an artefact of data fitting was investigated by carrying out a Monte Carlo simulation of the experiment. The correlation of the parameters of the simulated cell-survival curves was significantly less than the original set ($p < 0.05$).

Hill *et al* (1979) examined the radiation response of B16 melanoma cells. From a single-cell suspension of a subcutaneously grown tumour, clones were irradiated and subcultured until survival curves could be obtained. Positive correlation was found between the parameters of the fits of these data to the multi-target ($p < 0.01$) and quadratic ($p < 0.01$) formulae. The correlation is less impressive than for the SA12 lines, but the B16 clones do not arise from a homogeneous tumour. An equally good correlation ($p < 0.01$) is observed between the parameters of various animal and human melanoma cell lines.

On reviewing reported survival-curve parameters, the situation is much less clear for other cell lines such as HeLa. Factors which affect parameter values and might obscure possible relationships include changing from glass to plastic culture dishes—up to 40%, and RBE—up to 20%.

A relationship has been established between cell-survival-curve parameters of the SA12 lines which is not an artefact of formulation or data fitting, which has been found in melanoma lines and may be identified in other lines. It must be concluded that radiation response may not be a constant feature of a cell line which can display different survival characteristics under different conditions and after trauma.

REFERENCE

HILL, HELENE Z., HILL, G. J., MILLER, CATHIE F., KWANG, F. and PURDY, J., 1979. Radiation and melanoma: response of B16 mouse tumour cells and clonal lines to *in vitro* irradiation. *Radiation Research, 80*, 259–276.

---

*Now at Department of Dermatology, University of Glasgow, Glasgow G11 6NU.

RELATIONSHIP BETWEEN CELL-SURVIVAL PARAMETERS—A BIOLOGICAL INTERPRETATION

By G. F. Brunton and J. Kirk

West of Scotland Health Boards,
Department of Clinical Physics and Bio-Engineering,
11 West Street, Glasgow G4 9LF
and
Glasgow Radiobiology Group, Belvidere Hospital,
London Road, Glasgow G31 4PG

Observation of a correlation between two supposedly independent parameters characterizing three empirical cell-survival models (see previous abstract), neither explicable as a data handling artefact nor confined to a single cell line, has prompted reappraisal of the processes of radiation damage and repair.

For a simple model of damage these are: (1) random spatial distribution of radiation energy; (2) radiation damage assessed in terms of the number of hits received by individual cells; (3) only those cells with no hits at the time of measurement are clonogenic.

Two possible repair mechanisms have been investigated: (a) one simple way of incorporating repair requires that only cells having a number of hits equal to or less than some fixed threshold number can repair and are clonogenic. This predicts a shouldered survival curve where the surviving fraction is:

$$e^{-\lambda D}\sum_{i=o}^{m}\left(\frac{\lambda D}{i!}\right)^{i}$$

λ is the probability/unit dose that a cell receives 1 hit, D is the radiation dose, and m is the threshold number. This model has been fitted to the SA12 data described elsewhere giving significant fits in 8/12 sets ($p < 0.05$). Appropriate statistical analysis indicates that this model was comparable with the multitarget formulation but inferior to both quadratic and Green-Burki formulations in describing the SA12 survival data. However, the assumptions presented do not permit cells to repair only partially, a feature highlighted by an indication that non-integer threshold values would have yielded superior fits; (b) a more meaningful model of damage and repair requires the alternative assumption that there is a constant probability of repairing a hit, ρ, in the post-irradiation interval τ, independent of dose. This predicts a shouldered survival curve where the surviving fraction is:

$$\left\{e^{-\lambda D}\sum_{i=o}^{\infty}\frac{(\rho\tau\lambda D)^{i}}{(i!)^{2}}\Big/\sum_{j=o}\frac{(\rho\tau)^{j}}{j!}\right\}$$

Significant fits were obtained for 9/12 sets of the SA12 data and this model was compatible with the quadratic and Green-Burki formulations in its ability to describe the survival data. A strong linear correlation ($p < 0.001$) was found between damage and repair; between probability/unit dose that a cell receives 1 hit (λ) and the mean probability/unit time that a single hit is repaired (ρ). This model allows a more biological interpretation of the results than the more empirical models.

Consideration of the work of Sparrow *et al.* (1967) on the relation between multitarget D_0 and the chromosome volume, and the identification of a linear relation between λ and D_0 for the SA12 data, leads to the conclusion that radiation damage and repair may be linked through the chromosome volume.

REFERENCE

SPARROW, A. H., UNDERBRINK, A. G. and SPARROW, R. C., 1967. Chromosomes and cellular radiosensitivity. 1. The relationship of D_0 to chromosome volume and complexity in seventy-nine different organisms. *Radiation Research*, *32*, 915–945.

INTERACTION BETWEEN X RAYS AND NEUTRONS

By N. J. McNally and J. de Ronde

Cancer Research Campaign Gray Laboratory,
Mount Vernon Hospital, Northwood,
Middlesex HA6 2RN

V79 Chinese hamster cells have been irradiated with 250 kV X rays or neutrons generated by bombarding a thick beryllium target with 4 MeV deuterons produced in a 4 MV Van de Graaff accelerator. The survival-curve extrapolation numbers were approximately 10 for X irradiation and 1.8 for neutron irradiation. Cells exposed to a primary dose of X rays and then immediately afterwards to graded neutron doses regarded the X-ray dose as equivalent to an isoeffective neutron dose. When the order of radiations was reversed the cells regarded the neutron dose as less than an isoeffective X-ray dose. The resulting X-ray survival curve had a reduced shoulder with no change in the slope, but the shoulder was reduced by more than the shoulder to the neutron survival curve. These results imply that the order of the two radiations matters in determining the ultimate level of survival.

The interaction between X rays and neutrons when the X-ray dose was given first was used to measure RBEs at high levels of survival.

Preliminary results suggest that the RBE is about 4 at an X-ray dose of 0.25 Gy.

LINEARITY OF INDUCTION OF MICRONUCLEI AT LOW DOSES IN BEAN ROOTS

By I. Diehl-Marshall* and M. Bianchi

CERN, Geneva

The induction of micronuclei in the meristem of *Vicia faba* bean roots is a suitable effect for the study of damage produced by low doses (Diehl-Marshall and Bianchi, 1981). The beans were irradiated with ^{60}Co γ rays, neutrons produced by 600 MeV protons and neutrons from a ^{252}Cf source. The neutron data (lowest dose 0.2 cGy) are best fitted to a linear equation. The best fit to the γ data was obtained with a linear-plus-quadratic function, with the linear part being dominant in the region between 7 cGy and 20 cGy. Extrapolation to zero dose for all three curves resulted in values which coincide with the controls. Furthermore no dose-rate effect was observed for dose rates from 10 cGy/h to 500 cGy/h in this region. Constant RBE values were determined from the linear region. In the case of high-energy neutrons the value was found to be 36 ± 5 while for the ^{252}Cf neutrons it reached 75 ± 13.

REFERENCE

DIEHL-MARSHALL, I. and BIANCHI, M. Induction of micronuclei by irradiation with neutrons produced by 600 MeV protons. *British Journal of Radiology*, *54*, 530–532.

---

*Permanent address: Kernforschungszentrum, Karlsruhe, Institut für Kernphysik, 7500 Karlsruhe, Postfach 3640, Federal Republic of Germany.

THE EFFECT OF DEXAMETHASONE ON THE RADIATION SURVIVAL RESPONSE AND MISONIDAZOLE-INDUCED HYPOXIC-CELL CYTOTOXICITY IN CHINESE HAMSTER CELLS V79-753B *IN VITRO*

By Barbara C. Millar and Sally Jinks

Institute of Cancer Research,
Sutton, Surrey SM2 5PX

Overnight exposure of Chinese hamster cells, V79-753B, to μg quantities of the synthetic corticosteroid, dexamethasone, resulted in a decrease in sensitivity towards radiation, both in air and hypoxia. The effect was dose modifying and the oxygen enhancement ratio did not change appreciably. Similarly, when dexamethasone-treated hypoxic cells were irradiated in the presence of misonidazole, a hypoxic cell radiosensitizer, there was a decrease in radiation sensitivity compared with untreated hypoxic cells irradiated with misonidazole. The effect of dexamethasone cannot be attributed to classical radioprotection since administration of the drug immediately or 4.5 h before irradiation does not alter the survival response of hypoxic cells with or without misonidazole. Neither can this increased radioresistance be attributed to synchronization to a more resistant phase of the cell cycle since pretreated cells remain more radioresistant for at least 6 h after the removal of the drug. The data suggest that dexamethasone induces metabolic changes in cells which alter their radiosensitivity. Whatever metabolic changes may be occurring there was no effect on the uptake of ^{14}C-misonidazole into dexamethasone-treated or control cells. However, there was a pronounced decrease in hypoxic cell cytotoxicity induced by misonidazole in cells pretreated with dexamethasone. The implications of these results are discussed.

THE ENHANCEMENT OF EFFECT OF CHEMOTHERAPEUTIC AGENTS BY NITROIMIDAZOLES

By W. M. C. Martin and N. J. McNally

Gray Laboratory of the Cancer Research Campaign,
Mount Vernon Hospital, Northwood,
Middlesex HA6 2RN

The radiosensitizing drug misonidazole (MISO) has recently been shown to potentiate the cytotoxic effects of some chemotherapeutic agents, *i.e.* to possess a "chemosensitizing" ability. MISO has potentiated the action of melphalan and *cis*-platinum *in vitro* and the action of melphalan and cyclophosphamide (CY) *in vivo* in certain tumour systems. This paper describes work which investigates further the chemosensitizing effect of MISO in mouse tumours, and reports on normal-tissue toxicity in relation to white cell counts, LD_{50} and effects on the bladder. Two experimental assays have been used, tumour-cell survival and tumour growth delay. Cells from subcutaneous (SC) tumours of the tissue-culture-adapted sarcoma WHFIB were found to exhibit repair of potentially lethal damage (PLD) between 4 and 24 h after treatment by CY. 1 mg/g MISO given 1 h before CY inhibited this PLD repair and, independently, potentiated the cell kill at 4 h, so that potentiation of CY cytotoxicity was more marked at 24 h than at 4 h. When tumours were excised at 24 h after varying doses of CY, survival was an exponential function of dose. 1 mg/g MISO 1 h before CY was dose-modifying and gave a dose-modifying factor (DMF) of 2.1. Comparable effects were found using the regrowth delay assay. Other 2-nitroimidazole radiosensitizers also potentiated the action of CY. Ro 03-8799 was comparable to MISO as a chemosensitizer, but Ro 05-9963 was much less effective. Ro 12-5272 was effective at low concentrations, but is limited by its poor solubility. MISO given 6 h before CY, simultaneously, or even 2 h afterwards, caused significant potentiation of CY cytotoxicity, but MISO given 1 h before CY produced the optimum effect. There was a linear relationship between sensitizer dose and the regrowth delay following combined treatment. Since MISO has a short half-life in mouse tumours, the large effect seen when MISO is given 6 h before CY cannot be a function only of the amount of MISO in the tumour at 6 h after MISO injection. MISO also chemosensitized the action of melphalan on SC WHFIB tumours, as assayed by tumour cell survival at 4 h and at 24 h. When tumours were excised at 24 h after varying doses of melphalan, survival was an exponential function of dose. 1 mg/g MISO 1 h before melphalan was dose-modifying, with a DMF of 2.5. 2 mm WHFIB lung tumours did not exhibit repair of PLD after CY. They also showed a smaller degree of potentiation of CY cytotoxicity by MISO.

The effects on normal tissues have been generally encouraging: (1) The leukopaenia following 100 or 150 mg/kg CY was not significantly increased by 1 mg/g MISO 1 h earlier. (2) The $LD_{50/60}$ of CY in non-tumour-bearing WHT mice, 260 mg/kg, was altered by less than 10% by 1 mg/g MISO 1 h before the CY. (3) Measurements of urination frequency in mice following CY treatment showed an increase over untreated controls, which was reduced in mice who had 1 mg/g MISO 1 h prior to the CY. However, this result may be complicated by an effect on the fluid uptake of mice receiving the combined treatment.

Although the sensitizer doses used in this work were above those used in the clinic, significant chemosensitization has been achieved. The combination of a 2-nitroimidazole and a chemotherapeutic agent carries the potential for improving the treatment of metastatic disease.

A DIFFERENTIAL EFFECT OF MISONIDAZOLE ON THE CYTOTOXICITY OF CYCLOPHOSPHAMIDE IN TUMOUR AND NORMAL TISSUES

By Marilyn P. Law*, D. G. Hirst and J. M. Brown

Department of Radiology,
Stanford University School of Medicine,
California 94305, USA

The effect of misonidazole on the response of an experimental tumour and two normal tissues to cyclophosphamide was investigated in C3H/km mice.

Mice bearing RIF-1 tumours in the gastrocnemius muscle were given misonidazole (IP) before cyclophosphamide (IP). The response of the tumour was measured by growth delay and by cell survival estimated using a cloning assay at 24 h after the cyclophosphamide treatment.

The doses of misonidazole used (250–1000 mg/kg) had no effect on tumour growth or cell survival. Misonidazole, however, enhanced the cytotoxicity of cyclophosphamide as measured by both endpoints. For a single treatment, enhancement was maximal when misonidazole was given 0.5–2 h before cyclophosphamide. The enhancement ratio, defined as the dose of cyclophosphamide alone divided by the dose of cyclophosphamide with misonidazole required to cause a given effect, increased with increasing dose of misonidazole up to a maximum at 250 mg/kg. An enhancement ratio of 2 was observed when misonidazole (750 mg/kg) was given 30 min before doses of cyclophosphamide up to 50 mg/kg, but the enhancement ratio decreased to 1.3 as the dose of cyclophosphamide was increased to 150 mg/kg. For five daily treatments enhancement increased with cyclophosphamide dose up to 25 mg/kg per injection.

Survival of bone marrow stem cells at 24 h after injection of cyclophosphamide was measured using the spleen colony assay. Misonidazole (750 mg/kg) did not enhance the effect of lower doses (< 100 mg/kg) of cyclophosphamide, but a small enhancement (enhancement ratio 1.1–1.2) was seen for higher doses (100–200 mg/kg).

Circulating white blood cells were counted at four days after treatment when the depletion due to cyclophosphamide was maximal. The white-cell count was slightly lower when cyclophosphamide (20–200 mg/kg) was given 30 min after misonidazole (750 mg/kg) than when cyclophosphamide was given alone. A differential white-cell count showed that misonidazole had no effect on the response of lymphocytes to cyclophosphamide, but that the lowering of the total white-cell count could be accounted for by direct misonidazole cytotoxicity to neutrophils.

These experiments suggest that a therapeutic gain may be obtained by combining misonidazole with cyclophosphamide.

---

*Present address: MRC Cyclotron Unit, Hammersmith Hospital, Du Cane Road, London W12 0HS.

KINETICS OF RESPONSE TO IRRADIATION OF NORMAL TISSUES WITH DIFFERING PROLIFERATIVE ORGANIZATION

By T. E. Wheldon, J. Kirk and A. S. Michalowski

MRC Cyclotron Unit, Hammersmith Hospital,
London W12 0HS and Radiobiology Group,
Belvidere Hospital, Glasgow G31 4PG

It has been proposed that tissues can be separated into two categories (Michalowski, 1981). In type H (for "Hierarchical") tissues there exists a distinct clonogenic stem-cell compartment. The stem cells differentiate into irreversibly post-mitotic (mature) cells which perform tissue-specific functions. Irradiation initiates a depopulation of mature functional cells which proceeds at a steady rate independent of the dose but dependent on the steady-state kinetics (*e.g.* "turnover time") of the tissue. It is well-recognized for several tissues (*e.g.* bone marrow, GI tract) that the time of expression of damage to function is a constant independent of the dose.

In type F (for "Flexible") tissues, there is no distinct "stem cell" compartment but all cells are capable of proliferation and of performing tissue-specific functions. In this case, irradiation initiates a depopulation which begins slowly but accelerates as homeostatic compensatory proliferation reveals the lack of clonogenic capacity of radiation-sterilized cells. These processes follow a kinetic pattern in which the radiation dose is responsible not only for the magnitude of the damage to function inflicted, but also for the time of its expression: earlier expression occurs with higher doses.

Mathematical modelling of the response of a type F population confirms these qualitative features. Simulations incorporating reasonable values of the various parameters indicate that the time of expression of functional damage is dependent on dose only for relatively low doses (< 10–20 Gy) and that this dose-dependence is progressively lost at higher doses.

For some organs, experimental evidence indicates that the time of expression of damage is dose-dependent at considerably higher doses and that this may be due to another mechanism such as the capacity of clonogenically doomed cells to undertake a few divisions.

REFERENCE

MICHALOWSKI, A. S., 1981. Effects of radiation on normal tissues: hypothetical mechanisms and limitations of *in situ* assays of clonogenicity. *Radiation and Environmental Biophysics* (in press).

THE RESPONSE OF PIG SKIN TO NON-UNIFORM IRRADIATION WITH BETA-EMITTERS OF VARYING ENERGY

By D. M. Peel and J. W. Hopewell

Churchill Hospital Research Institute,
University of Oxford

In a study of the non-stochastic effects of β-emitters on pig skin, the acute reactions after ^{90}Sr ($E_{\max}$ 2.27 MeV, range in tissue 8.0 mm) and ^{170}Tm ($E_{\max}$ 0.97 MeV, range in tissue 3.2 mm) irradiations were observed. Strontium produced the characteristic two-wave response, a first wave from weeks 1–9 with a maximum reaction of bright red erythema and moist desquamation, and a second wave from weeks 10–16 with maximum reaction mauve erythema and dermal necrosis. Thulium irradiation produced only the first wave of the reaction.

This supports the theory that the first wave is due to the epithelial response, *i.e.* damage to the basal-cell layer and the papillary plexus of blood vessels, and the second wave is due to damage to the deep dermal plexus of vessels which receives a low dose from the lower energy thulium irradiation.

Irradiations with a 2 cm diameter strontium source produced a given epithelial reaction at approximately half the dose required from a 1 cm source, while thulium showed no difference in response between the two sizes. This is explained by the high proportion of surviving epithelial cells in the hair follicles and rete-pegs.

GASTRO-INTESTINAL LESIONS IN THORAX-IRRADIATED MICE

By A. S. Michalowski

MRC Cyclotron Unit, Hammersmith Hospital,
London W12 0HS

The thorax of five-week-old female HC/CFLP mice was irradiated with a single dose of 14 Gy fast neutrons. Of 149 mice, 144 (97%) died during the first 28 days after exposure. Death at this time has generally been assumed to be due to radiation oesophagitis and its complications (Phillips and Ross, 1974). The remaining five mice died by day 55. All the animals were submitted to post-mortem and microscopic examination. Unexpectedly, three modes of mortality were seen, their peak times occurring at days 5, 10 and 20. This finding alone was suggestive of multiple causes of death. In the 144 mice which died during the first four weeks after thoracic irradiation, ulcerative oesophagitis was found at death in 95 (66%), and was complicated by perforation of the oesophagus in 12 animals (8%). Some other autopsy findings included the presence of plant material (presumably food particles) in the lumen of trachea and bronchi (18%), bronchopneumonia (15%), and the denudation of bronchi with diffuse pneumonitis (40%). A totally unexpected finding was the presence of duodenal/gastroduodenal ulcer (30%), ulcerations of the small (15%) and large intestines (7%) and melaena (31%). The dose of scattered neutrons to organs of the epigastric region was 13% of that in the centre of the radiation field, *i.e.* less than 2 Gy. This figure, as well as the sharp delineation of the ulcers (which are not a normal response to irradiation) surrounded by normal mucosa, suggested that the observed gastrointestinal lesions fell into the category of abscopal effects of radiation. Although less detailed experiments have been performed with X rays, the general pathological features are similar after low LET radiation.

In a separate experiment 23 out of 24 adult female CFLP mice irradiated to their thorax with 16 Gy or more of X rays developed duodenal or gastroduodenal ulcer by day 9 ± 1 after exposure, while none was seen in 20 animals exposed to 13 Gy or less. A similar dose-dependence was observed at six weeks.

REFERENCE

PHILLIPS, T. L. and ROSS, G., 1974. Time–dose relationships in the mouse oesophagus. *Radiology*, *113*, 435–440.

The British Institute of Radiology Awards 1981

The following awards have been made by the Council of the British Institute of Radiology and were presented at the Annual Dinner of the Institute on Thursday, 9th April, 1981.

The Barclay Medal to Dr. H. M. Saxton, of Guy's Hospital, London, for outstanding contributions to diagnostic radiology particularly in the field of the urinary tract.

The Barclay Prize to Dr. D. R. White of St. Bartholomew's Hospital, London for his contributions to the physical aspects of diagnostic radiology.

The Röntgen Prize to Professor D. M. Taylor of the Institute for Genetics and for Toxicology of Fissile Materials, Karlsruhe, Germany for his contribution on the metabolism of plutonium-239 and of various radiopharmaceuticals in animals and in man.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Fellowships and Grants for Cancer Research

The International Union against Cancer invites applications for: Cancer Research Campaign fellowships (deadline October 1); Eleanor Roosevelt International Cancer fellowships (deadline October 1); Yamagiwa-Yoshida Memorial International Cancer Study grants (deadline December 31); and International Cancer Research Technology Transfer Programme grants (applications as soon as possible). Details and application forms from: UICC, rue du Conseil-Général 3, 1205 Geneva, Switzerland.

International Symposium and Course on Abdominal Ultrasound

Turku, Finland, August 10–12, 1981, organized by the Radiological Society of Finland and the European Association of Radiology. Language: English. Guest speakers: C. R. Hill, H. H. Holm, M. Johnson, A. Kratochwil, C. Metreweli, E. H. Smith and F. Weill. Two "free communications" sessions, for which 10 minute papers are invited: abstracts to be submitted with registration. Technical exhibition and social programme. Information and registration: Oy Konfer Ab, Yliopistonkatu 29 c B, SF-20100 Turku 10, Finland.

Society of Nuclear Medicine Europe
19th Annual Congress

September 8–11, 1981. Information: President Dr. H. Rösler, Department of Nuclear Medicine, Inselspital, 3010 Bern, Switzerland.

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275-2617.

Skeletal Radiology

The Eighth Refresher Course of the International Skeletal Society will be given in Madrid, Spain, September 25–27, 1981.

For further information, please write to: A. Bonakdarpour, M.D., Department of Diagnostic Radiology, Temple University Hospital, 3401 North Broad Street, Philadelphia, PA 19140, USA; or Prof. Dr. Friedrich W. Heuck, Zentrales Röntgeninstitut, Katharinen Hospital der Stadt Stuttgart, Kriegsbergstrasse 60, Stuttgart 1, Germany.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

The Faculty of Radiologists of The Royal College of Surgeons in Ireland

21st Anniversary Meeting, Dublin, October 2–3, 1981: jointly with The British Institute of Radiologists, The Royal College of Radiologists, and The Royal Society of Medicine. Diagnostic and therapy sessions; topics to include radiology in renal failure and radiology of trauma. The BIR Presidential Address for 1981, "Chest radiology—guesswork or science?" will be given by Dr. D. H. Trapnell. Technical exhibition. Details: Miss A. Daly, Faculty of Radiologists, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Diagnostic Imaging in Medicine Course

October 11–23, 1981, Estoril, Portugal. Sponsored by NATO Advanced Study Institute and The George Washington University Medical Center. Registration $95.00 (no other charge). CME Category I credits available. Subjects include: nuclear, ultrasound, CT, NMR, and X-ray imaging, clinical and experimental. For application to attend write: Richard C. Reba, M.D., Division of Nuclear Medicine, George Washington University Hospital, 901 Twenty-Third Street, NW, Washington, DC, 20037. Phone: (202) 676-3458.

Royal College of Physicians and Surgeons of Glasgow Symposium on "Choices in Organ Imaging—When to do What"

This symposium will be held in Glasgow on Wednesday, October 14, 1981. Chairmen: Dr. J. K. Davidson, Dr. W. B. James and Dr. J. G. Duncan. Speakers: Dr. S. R. Wild, Dr. E. Barnett, Dr. D. A. R. Robertson, Dr. J. C. Rodger, Prof. I. Isherwood, Prof. J. J. K. Best, Dr. M. V. Merrick and Dr. P. Morley. Registration fee £10. Applications and information: The Hon. Secretary, Royal College of Physicians and Surgeons of Glasgow, 234–242 St. Vincent Street, Glasgow G2 5RJ (phone 041-221 0241).

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Forthcoming events and notices

Radiobiology Work-in-Progress Meetings

Meetings during the coming year at the Institute include "Subcellular targets, including ultrastructural damage", November 20, 1981; a general meeting on February 26, 1982 and "Late damage to normal tissues after radiotherapeutic doses" on May 21, 1982. The all-day Saturday meeting will be on November 21, 1981, on "The effects of small doses—the basis of radiation protection".

Please note all meetings will be held at the BIR's new address, 36 Portland Place, London W1.

The Radiological Diagnosis and Treatment of Thyroid Disease
Wednesday, November 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held in London (venue to be announced). The meeting will cover all aspects of thyroid disease, including the use of isotopes. There will be some invited speakers but proffered papers are invited and should be sent to: Dr. John Frank, The Wessex Regional Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY before August 31, 1981.

Safety Review and Inspection of Nuclear Power Plants

The International Atomic Energy Agency will hold a seminar in Vienna from November 23–27, 1981. Further information and participation forms from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4OJ (phone 01–211 6850). Abstracts of proffered papers by August 14, applications by September 30.

Paediatric Radiology 1981
Great Ormond Street, London, November 26–27

This annual two-day course is designed for consultants and senior registrars. The theme will be the gut; other topics covered will include jaundice, hypertension and the neonatal big head. Speakers will include paediatricians, paediatric surgeons and endoscopists; there will be opportunity for open discussion.

There are a limited number of places. Cost £40. Full details: Dr. I. Gordon, Department of Paediatric Radiology, Hospital for Sick Children, Great Ormond Street, London WC1 (telephone 01–405 9200).

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1. Proffered papers are invited; abstracts should be sent to Dr. W. Hately, X-ray Department, London Hospital, Whitechapel, London E1 1BB to arrive not later than August 31, 1981.

6th Carvat International Meeting on Body CT and New Imaging

This meeting, organized and directed by Plinio Rossi, M.D. and Roberto Passariello, M.D., will be held in Rome from February 1–5, 1982, at the Hilton Hotel. The programme is based on technical and clinical advances in ultrasound, fast body CT and new imaging (digital angiography, nuclear magnetic resonance, emission tomography, etc.). A limited number of proffered papers will be accepted after evaluation.

Lectures will be given by European and American guest speakers: R. Alfidi, A. Baert, E. Buonocore, A. Crummy, P. Dean, W. Frommhold, W. Fuchs, C. Lachner, J. L. Lamarque, M. Lipton, T. Meaney, L. Ovitt, C. Pedrosa, N. Schad, P. Sheedy, M. Ter-Pogossian, A. Van Voorthuisen and M. Wholey. Official languages will be English and Italian with simultaneous translation. Registration fee: $140 before November 30; $200 afterwards.

Information: Plinio Rossi M.D., 2a Cattedra Istituto di Radiologia, Policlinico Umberto 1, 00161 Roma, Italy.

International Symposium on Computed Tomography "CT '80"

The Department of Radiology, University of Munich and the Department of Diagnostic Radiology, National Institute of Health, Bethesda USA, will present an International Symposium on Computed Tomography from January 28–30, 1982, at Seefeld Tyrol, Austria. Topics to be discussed will be pelvis, mediastinum, high densities, contrast medium and CT craniocervical and spinal CT. There will be simultaneous translation in English and German.

For further information, contact Prof. Dr. J. Lissner, Radiologische Klinik, Klinikum Grosshadern der Universität München, Marchioninistrasse 15, D-8000 München 70.

The Mayneord Symposium

Friday, February 19, 1982. This meeting is being organized by, the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. It will be an all-day meeting to be held at the Royal Society, in Carlton House Terrace, London. The theme for the meeting will be "The future in radiology" as seen by distinguished workers in a number of branches of radiological science.

Society for Radiological Protection
Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ. Abstracts to be received by July 15, 1981.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on The contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A.

M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

5TH SOUTH AFRICAN INTERNATIONAL RADIOLOGICAL CONGRESS

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas sponsors, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

Book reviews

Endoscopy and Biopsy in Gastroenterology. Technique and Indications. Edited by P. Frühmorgen and M. Classen, pp. vi+198, 1980 (Springer-Verlag, Heidelberg), DM.28.
ISBN 3-540-09645-0.

The sighs of relief given out by the Treasurers of our Health Districts were almost audible after the first wave of enthusiasm following the introduction of fibre optic gastrointestinal endoscopy had passed. The technique is now well established in most large hospitals in the UK, even though the exact role of these procedures in some clinical situations has yet to be established. But gastrointestinal endoscopy should not be treated as a subspecialty in its own right, but rather as one other technique which is available to help in the management of various gastrointestinal problems. As such, all potential gastroenterologists (and perhaps radiodiagnosticians??) should now expect their training programmes to include experience in this field. It is to this group of doctors-in-training that this book seems largely directed.

Although designed as a pocket book for rapid reference, it is difficult to imagine our would-be endoscopist holding the open book in his left hand while trying to navigate a colonoscope round a splenic flexure with his right. There can, of course, be no substitute for a comprehensive, supervised, practical training in an experienced gastrointestinal unit, but the trainee will nevertheless find this book very useful if he reads it before starting his practical experience.

The whole field of fibre optic endoscopy, from mouth to anus, is covered in this volume, including the much neglected (at least in the UK) field of laparoscopy. The book strays, perhaps unnecessarily, into the old-established and well-tried fields such as liver or jejunal biopsy. There are excellent chapters, such as that on colonoscopy, giving details of manipulative technique which will be invaluable to the trainee. But this contrasts sharply with the somewhat perfunctory dismissal of some important areas such as gastrointestinal haemorrhage.

The rigid format of this work appears to be unnecessary at times, but it does facilitate the book's declared intention which is to be used as a reference manual. The book's teutonic origins are further betrayed by the frequent use of adjectives such as "essential" and "obligatory" when, in most instances cited, our Anglo-Saxon reader may regard "desirable" or "useful" as more appropriate. Similarly, regional and cultural differences in medical practice must make our trainee question at least some of the stated indications or contraindications. For example, he may question if X-ray negative constipation is really an absolute indication for colonoscopy. The thought of a little old rheumatoid lady with an unstable neck may lead him to believe that haemorrhagic shock could not be the only contraindication to emergency endoscopy in gastrointestinal bleeding. He may not be persuaded that to convince a patient of the need for gall-bladder surgery is a good indication for laparoscopy, and he may prefer to believe that those who premedicate with atropine do so for reasons which are other than medicolegal.

However, the editors do not claim that their book is anything other than an expression of opinions by the authors. Since those authors represent the most respected and experienced professionals in their fields, we should all wish to read these opinions. I cannot help feeling that the book would have a much wider appeal to more experienced gastrointestinal diagnosticians if the authors had allowed themselves a little more discussion of less clear-cut issues, *e.g.* the appropriate use of antibiotics following bile duct cannulation, or the timing of emergency endoscopy after bleeding. But such feelings may be unrealistic if the advantages of clarity and brevity are to be retained.

Buy the book. Your registrars will thank you.

R. E. BARRY.

Nuclear Particles in Cancer Treatment. By J. F. Fowler, pp. xii+178, 1981 (*Medical Physics Handbooks. 8*) (Adam Hilger, Bristol), £11·95.
ISBN 0-85274-521-4

This volume is intended "for cancer research workers, for medical physicists and engineers interested in heavy-particle radiotherapy and for radiotherapists and radiographers". However, it should be of interest also to a considerably wider audience since it is topical, it does not assume specialized knowledge and it is written in a clear, concise and very readable style. After a general introduction to the treatment of cancer, by radiation in particular, it explains how some of the limitations of conventional radiotherapy with gamma rays or X rays may be reduced by the use of beams of nuclear particles. In comparing the merits of the various possible heavy-particle beams it highlights the excellent physical dose-distributions achievable with protons, the greatly increased biological efficiency of killing hypoxic cells by neon and argon ions, the more modest improvements in both respects with carbon ions and negative pi mesons, and the much lower cost, yet desirable biological properties, of fast neutrons.

The uses of such beams are in various stages of experimental development ranging from early pilot studies to extensive clinical trials. The reader is bound to feel the author's optimism and to share his hope that future clinical trials will show highly significant improvements in cancer treatment by the new beams.

Any criticisms of the book would be trivial in comparison with its merits. Some reservations stem from simplifications which are inevitable in a book of this scope, but the well-selected reference list will guide the reader to any area chosen for study in greater length. The book is to be highly recommended.

D. GOODHEAD.

Book reviews

Influence of Dose and its Distribution in Time on Dose-Response Relationships for low-LET Radiations. Recommendations of the National Council on Radiation Protection and Measurements (NCRP Report 64), pp. vi+216, 1940 (NCRP, Washington), $9.00.
ISBN 0–913392–48–0

Knowledge of the biological effects of radiations received at low doses and particularly at low dose rates is of crucial importance in the assessment of radiation hazards to human populations. However, it is in this area that radiobiological information is at its scarcest and most tantalizing. Many data have been collected, but for those who are responsible for radiation protection and evaluation of the risks involved many questions remain to be answered.

The appearance of this report by the NCRP of the United States is timely, and its summary of the field along with its recommendations is of immense value to those interested in the theoretical, experimental and practical aspects of dose-rate effects. Discussion is limited to effects caused by low-LET radiations, but as these are the radiations of which dose rate is of critical relevance, the focus is on the main area of current importance.

The report opens with a brief introduction on the shapes of possible dose-response curves and the influence of dose rate, and develops this theme further with specific reference to the response of *Tradescantia* to mutation induction. As might be expected, the main emphasis of the report is on the induction of chromosomal changes, point mutations, cell transformation and carcinogenesis, both in experimental and human populations. This provides an up-to-date and comprehensive picture of current knowledge that is very well done considering the relatively short length of the report. Discussion is also included on the influence of low doses and dose rates on various tests of damage in plants, injuries in growth and development of the mammalian embryo following prenatal irradiation, and on effects on life span. An extensive list of references is given at the end of the volume.

The final chapter on the conclusions to be drawn from the analysis of the data presented earlier is, of course, the most interesting. These are reached on the basis of the shapes of the possible dose-response curves and on the estimated values of dose-rate effectiveness factors (DREF). The DREF is "the factor by which linear interpolation from data obtained at high doses and dose rates overestimates the risk per unit absorbed dose of radiation delivered at very low doses and/or dose rates". Perhaps the most important conclusion is that for intermediate and low doses the data are still not sufficient to define the shape of the dose-response curve for cancer induction in humans, and the available evidence suggests that DREF has a value between 2 and 10. Thus, more measurements are urgently required. There seems little doubt that for human subjects there is no threshold for mutagenesis and carcinogenesis.

This little volume gives an excellent summary of the field it describes and is essential reading for all interested in the subject from whatever point of view.

N. E. Gillies.

Fundamentals of Radiation Dosimetry. By J. R. Greening, pp. xii+160, 1981 (Medical Physics Handbooks. 6) (Adam Hilger Ltd., Bristol), £10·95.
ISBN 0–85274–519–2

This book by Professor Greening is a most welcome addition to the series of medical physics handbooks organized by the Hospital Physicists' Association. It is an excellent sequel to an earlier book "Principles of radiation dosimetry" by G. N. Whyte which was published in 1959. The two books are of similar length and cover very much the same ground but Whyte's book is now out of date due to the introduction of the SI units of radiation. Many of the diagrams in Whyte's book reappear in Greening's, indicating a continuity which will reassure many of us who admired the earlier book.

The new one is concerned mainly with the measurement of radiation quantities using ionization chambers. Other techniques such as calorimetry and TLD are not, however, neglected. The first group of chapters discusses the basic quantities used to describe the radiation field, together with the interactions between radiation and matter. X and γ rays, electrons and neutrons are included. Subsequent chapters discuss in detail the measurement of kerma, exposure and absorbed dose. The final chapters are concerned with radionuclides, various techniques of dosimetry and applications in radiation protection. Throughout, everything is explained with the greatest clarity and economy of expression.

The book stops short of giving the dosimetrist detailed instructions for practical measurements. It was, however, a surprise to me to find no mention of the factors C_λ and C_E which are used to determine the sensitivity of an ionization chamber to high-energy photons and electrons, based on a calibration with 2 MV X rays, particularly as Professor Greening has been so closely concerned with the proper derivation and use of these factors. Perhaps he felt at the time of writing that the details were still subject to revision.

This book is essential for anyone wishing to understand the basis of the methods used in radiation dosimetry. There need no longer be any excuse for confusion between absorbed dose, kerma and exposure, or absorbed dose, dose-equivalent, RBE and quality factor.

D. K. Bewley.

Mammography. Recommendations of the National Council on Radiation Protection and Measurements. NCRP Report No. 66, pp. v+85, 1980 (National Council on Radiation Protection and Measurements, Washington), $7.00.
ISBN 0–913392–51–0

The value of mammography in symptomatic patients is now well established, but its use as a mass screening technique for asymptomatic women is still controversial.

In the fourth chapter of this report, the National Committee on Radiation Protection and Measurements of the USA tries to provide a considered view on relative risks and benefits of mammography. An earlier chapter also contains some very useful descriptions of equipment and techniques and the measurements that should be performed to ensure that equipment is operating satisfactorily.

The values of carcinogenic risk based on data for Western women over age 20 at exposure are estimated to be, on a relative basis, 0.42 per cent per rad, and on an absolute basis 6.6 cases per million women per year per rad. The mid-plane dose can be kept below 0.5 rad per exposure and, using the most sensitive film-screen combinations and a molybdenum target, the mid-plane dose can be further reduced by an order of magnitude. Nevertheless, evidence on which to make a risk/benefit assessment is still not clearcut for women under 50, and the report concludes that "use of the examination as a screening procedure in women under age 50 cannot be recommended".

This report will be of interest and value to all clinicians concerned with mammography, and will also be useful to a physicist who needs to carry out quality-control measurement on mammographic apparatus.

J. L. Haybittle.

Book reviews

Hodgkin's Disease. By Henry S. Kaplan, 2nd edit., pp. xiv + 689, 1980 (Harvard University Press, London), £30·00. ISBN 0-674-40485-8

Few subjects in cancer medicine have excited so much interest or activity over the past decade as the investigation and treatment of Hodgkin's disease. This enthusiasm is reflected in the wealth of published material which has recently become available on all aspects of the disease. This second edition of Dr. Kaplan's excellent book is, therefore, both timely and extremely welcome. The text now numbers in excess of 600 pages but the improved typeface and orderly presentation make it a very easy book to read.

As in the first edition, the book is based on studies conducted at the Stanford University Medical Centre but a quick glance at the impressive reference list shows that Dr. Kaplan has reviewed and assimilated a huge volume of data from other workers into a comprehensive and critical analysis, covering every facet of the disease from the aetiology and pathology to treatment and prognosis.

Much of the recent laboratory research effort has been directed towards attempts to characterize the Sternberg Reed cell and to define more clearly the nature of the immunological deficiency observed in many of these patients; the section dealing with cell mediated immunity has more than doubled in size to take account of the information currently available.

The approach to investigation in patients with Hodgkin's disease begins with chapter 4 which is concerned with clinical evaluation. This leads to an enlarged chapter on X-ray and isotope diagnosis, which now includes consideration of the role of computerized tomographic scanning. As before, this chapter contains clearly marked and beautifully reproduced illustrations and shows in detail the common and more unusual presentations seen on chest radiography, lymphangiography, skeletal survey or isotope scanning.

The chapter on radiotherapy begins with an historical review and a discussion of the rationale behind modern radiotherapeutic practice. Treatment planning and therapy techniques, as employed at Stanford, are described in precise detail together with the potential complications of irradiation and the means by which many of these may be avoided. In the historical review the name of Dr. N. S. Finzi is again omitted, which seems a pity since he was surely the first in his treatise "Radium therapeutics" (published in 1913) to suggest the potential benefit of prophylactic irradiation administered to clinically uninvolved lymph node groups. There follows a discussion of the chemotherapy of Hodgkin's disease, detailing the effective single agents and the many combination regimes and their remission rates. Again attention is drawn to the potential complications of cytotoxic chemotherapy, including infertility and the hazard of second malignancies.

The major objective in the management of Hodgkin's disease in the next ten years will be the development of treatment programmes which, while maintaining or increasing their efficacy in terms of survival, will, at the same time, allow a reduced incidence of immediate or delayed toxicity. By the addition of a chapter on the selection of optimal treatment, Dr. Kaplan has addressed himself to this problem and has set out a series of treatment recommendations based on currently available data. At this point he states, quite openly, that these recommendations represent the best clinical judgement at this time and that clearly modification of treatment programmes will be necessary as more information becomes available with prolonged follow-up. While not everyone will agree with the proposals outlined, a detailed summary of the results of treatment for individual stages and clinical situations based on the Stanford series is included and is essential reading for all those intimately involved in clinical decision making.

In short this is an outstanding book which must be regarded as the definitive work on the subject. It stands as a tribute to the enormous personal contribution made by Dr. Kaplan both in the investigation and treatment of Hodgkin's disease. No radiotherapy or oncology department should be deprived of a copy since anyone who takes time to consult it will not come away disappointed.

ADRIAN R. TIMOTHY.

Books received

We would like to thank the publishers for sending copies of the following, which have been placed in the Library of THE BRITISH INSTITUTE OF RADIOLOGY for the use of members.

International Agency for Research on Cancer. *Annual Report, 1980*. pp. 202. (WHO) $7.00 Sw.fr.12. (IARC, Lyon). ISBN 92-8-321080-8.

Les Accessoires en Radiothérapie externe. Société des Physiciens d'Hôpitaux d'Expression Française, Cahier No. 15. pp. 32. 1980. (SPHEF, Paris), Fr.55.

Specification for Personal Photographic Dosemeters—British Standards Institution. BS 6090: 1981.

New journals

European Journal of Radiology. Editors-in-Chief: H. Anacker (München), J. H. Göthlin (Bergen), J.-L. Lamarque (Montpellier) and G. F. Pistolesi (Verona). Vol. 1, No. 1, March 1981 (Georg Thieme Verlag, Stuttgart/New York). In English. Annual subscription DM.148 plus postage (single copies DM.44.50 plus postage): enquiries to Georg Thieme Verlag, PO Box 732, D-7000 Stuttgart 1, Germany.

Clinical Physics and Physiological Measurement. Issued quarterly by the Hospital Physicists' Association and the Deutsche Gesellschaft für Medizinische Physik and published by the Institute of Physics, Bristol, in association with the American Institute of Physics. Honorary Editors: M. M. Black and P. H. Fentem. Vol. 1, No. 1, February 1980. Annual subscription £50 (USA, $115.00).

Correspondence—*continued.*
Preparation for barium enema.
J. G. B. Russell
Calcification of the posterior longitudinal ligament of the spine.
I. Dinakar

Obiturary: J. D. Frye 701

Proceedings of The British Institute of Radiology, February 1981. 702
Radionuclides in gastroenterology.
Combined radiotherapy and chemotherapy: advantages, disadvantages—can radiobiology help?
Radiobiology work-in-progress meeting.

The British Institute of Radiology Awards 1981. 713

Forthcoming events and notices. 714

Book reviews

Radiology of bone disease 650
Renal microvascular disease angiographic-microangiographic correlates 654
Induced disease — drugs, irradiation, occupation 659
An introduction to diagnostic ultrasound 664
Clinical ultrasound review 664
Ultrasonically guided puncture technique 670
Cases in diagnostic ultrasound. 1 670
Endoscopy and biopsy in gastroenterology 716
Medical physics handbooks 8. Nuclear particles in cancer treatment 716
Influence of dose and its distribution on dose-response relationships (NCRP Report 64) 717
Medical physics handbooks 6. Fundamentals of radiation dosimetry 717
Mammography (NCRP Report 66) 717
Hodgkin's disease 718

Books received 718

New journals 718

Treatment Simulators

British Journal of Radiology Supplement 16, 1981

This is a revised version of a working-party report which was first published in 1976 as BIR Special Report 10, and owing to heavy demand has been out of print for some time. The authors consider the place of planning simulators in modern radiotherapy and endeavour to set up guide lines for their future development, covering both specifications for the instruments and the ways in which they are used. The report also discusses the relationship between simulators and transverse axial computed tomography.

The report has been fully updated and is highly detailed, containing 31 pages, 10 figures, and 59 references covering the period 1952 to 1981. The Convenor of the Working Party was C. K. Bomford and other members were Miss L. M. Craig, F. A. Hanna, G. S. Innes, S. C. Lillicrap and the late R. L. Morgan, with G. R. Higson as DHSS Observer.

Of practical interest to all involved with developments in radiotherapy.

ISSN 0306–2120 Price £3.50

Orders to:

Publications Department, The British Institute of Radiology,
32 Welbeck Street, London W1M 7PG;
or through your bookseller.

VOL 54 NO 644 AUGUST 1981

The British Journal of Radiology

Contents

Page

Round (helical) atelectasis. 643
S.-R. Cho, D. A. Henry, M. C. Beachley and J. W. Brooks

Benign greater curve gastric ulcer: the "sump-ulcer". 651
R. E. Kottler and R. J. Tuft

Pre-operative computed tomography of carcinoma of the rectum. 655
A. K. Dixon, I. Kelsey Fry, B. C. Morson, R. J. Nicholls and A. York Mason

Ultrasound measurement of fetal limb lengths. 660
Pat Farrant and Hylton B. Meire

Ultrasonically guided percutaneous interstitial implantation of iodine 125 seeds in cancer therapy. 665
H. H. Holm, I. Strøyer, H. Hansen and F. Stadil

Technical notes. 671
- A catheter system for the safe and efficient delivery of tissue glues (bucrylate) for visceral embolization.
  M. S. Khangure, H. T. ApSimon, T. M. H. Chakera and D. E. Hartley
- Longitudinal emission tomographic imaging using a three-pinhole operture and an Anger camera.
  S. Webb

Case reports. 678
- Combined duodenoscopic and transhepatic approach to stenosis of the papilla of Vater.
  R. R. Mason and P. B. Cotton
- Biliary sludge—ultrasonic appearance simulating neoplasm.
  B. Anastasi and G. R. Sutherland
- An unusual case of subcutaneous emphysema.
  S. A. Thompson, J. S. Harper and P. Millican
- Giant diverticulum arising from the transverse colon of a patient with diverticulosis.
  K. J. Wallers
- Pseudo tumours of the colon due to adhesions.
  Z. F. Boulis and D. R. Osborne
- Pre-natal ultrasound demonstration of lymphangiectasia in the mesentery of the small bowel.
  K. C. Dewbury, K. S. Rao and V. Poll
- The diagnosis by computerized tomography of a parathyroid adenoma presenting as acute pancreatitis.
  N. R. McLean, N. C. McMillan and J. G. Duncan

Correspondence. 691
- The "ten-day rule".
  M. L. Ramsdale
- A "new line" in radiology.
  A. Karle and E. B. Hansen
- The incidence of headache following various techniques with metrizamide myelography.
  J. P. de V. van Niekerk; E. B. Rolfe
- Blood flow rate determination using computed tomography.
  L. M. Zatz; K. A. Tonge
- The Dalkon Shield.
  W. D. Savage
- Migration of localizing wire into pleural cavity.
  E. J. Roebuck; M. J. Homer; J. B. Bristol
- Para-aortic nodes in carcinoma of the cervix.
  I. J. Kerby; J. S. Macdonald
- Radiation hazards.
  P. R. J. Burch
- The relationship of dose to prognosis in squamous cell carcinoma of the aerodigestive tract.
  W. E. Liversage; M. Wollin and A. R. Kagan
- Radiation doses in neutron therapy.
  J. P. Geraci; Shirley Hornsey

(continued on inside back cover)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
32 Welbeck Street, London W1M 7PG

ISSN 0007-1285
16979

11·1·82

September 1981

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis
Radiation oncology
Nuclear medicine
Ultrasound
Radiological physics
Radiobiology
Radiation protection
and related disciplines

Published b
The British Institute of Radiolog

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

J. L. HAYBITTLE, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., CH.B., F.R.C.R., F.R.A.C.R. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01-836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14).

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
36 PORTLAND PLACE, LONDON W1N 3DG
Telephone: 01-935 6237 and 01-935 6867. Cable Address: "Britology, London W.1."

President: D. H. TRAPNELL, M.A., M.D., F.R.C.P., F.R.C.R., D.M.R.D.

Hon. Secretaries:
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
H. B. MEIRE, M.B., B.S., M.R.C.S., L.R.C.P., F.R.C.R., D.OBST., R.C.O.G., D.M.R.D.

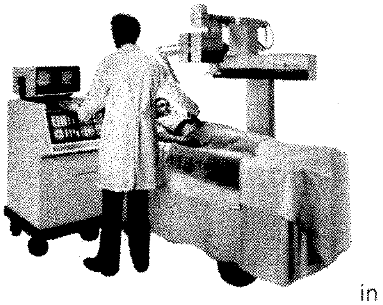
Hon. Treasurer: D. T. KERRISK
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company offers computer-integrated ultrasound with superior B-scan and real time images?

General Electric Company of U.S.A:*
Images that maximize diagnostic data.



All ultrasound images from the Datason system—whether B-scan, linear array real time or real time sector scans—are processed through the system's microcomputer. Resulting enhanced images maximise diagnostic usefulness.

In addition, General Electric U.S.A. offers Dataline—a linear array real time system which brings a new standard of image quality to stand-alone, real time ultrasound.

Such high quality images are integral with every GE U.S.A. imaging system.

For example, in computed tomography, CT/T system's ReView retrospective image analysis capability provides spatial resolution of 0.6mm for bone detail; in conventional radiography/fluoroscopy, the Fluoricon L300 image intensifier provides state-of-the-art image quality; and, in nuclear diagnostics, the MaxiCamera 535 system detector features 61 hexagonal teacup photomultiplier tubes for improved linearity, and extra-large 530 mm field of view.

Superior images. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

Frankfurt/M., Tel.: 06 11/7 60 73 69 • Wien, Tel.: 24 14 51 • Brüssel, Tel.: 660 2010 • Kopenhagen, Tel.: 2 86 86 00 • Mailand, Tel.: 753 1351 •
Breda, Tel.: 76 22 54 15 • Lissabon, Tel.: 36 71 55 • Madrid, Tel.: 252 5100 • Goteborg, Tel.: 42 09 70 • Zurich, Tel.: 47 50 30

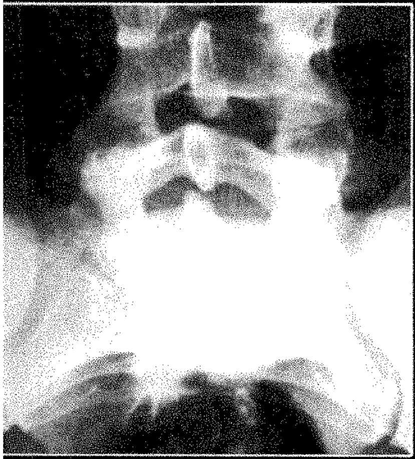
International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

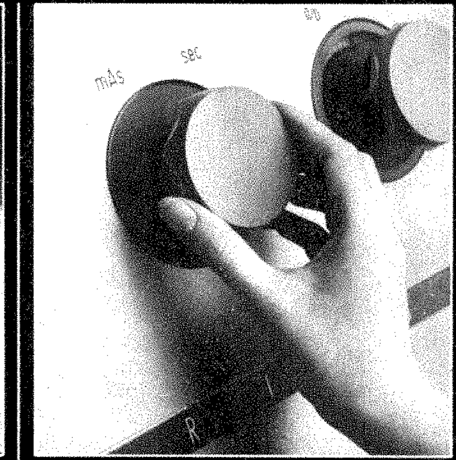
GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

THE 3M TRIMAX SYSTEM:

THREE WAYS BETTER





1. Finer diagnostic quality.
he gadolinium oxysulphide formulation used exclusively by the 3M rimax System ensures:
- a) better definition from this high efficiency phosphor
- b) less graininess from a finer, more regular grain structure
- c) better image characteristics by reduced probability of scatter.

2. Less exposure time.
The Trimax System is faster - up to 90% faster than conventional systems. This means:
- a) less radiation dosage,
- b) less chance of patient movement,
- c) greater use of fine focus.

3. Longer operating life.
Trimax screens, the first of which were introduced in 1974, have yet to show any loss of speed.

That's why they all come with an exclusive 7-year guarantee against loss of speed.

That's why replacement ceases to be a factor with the Trimax System.

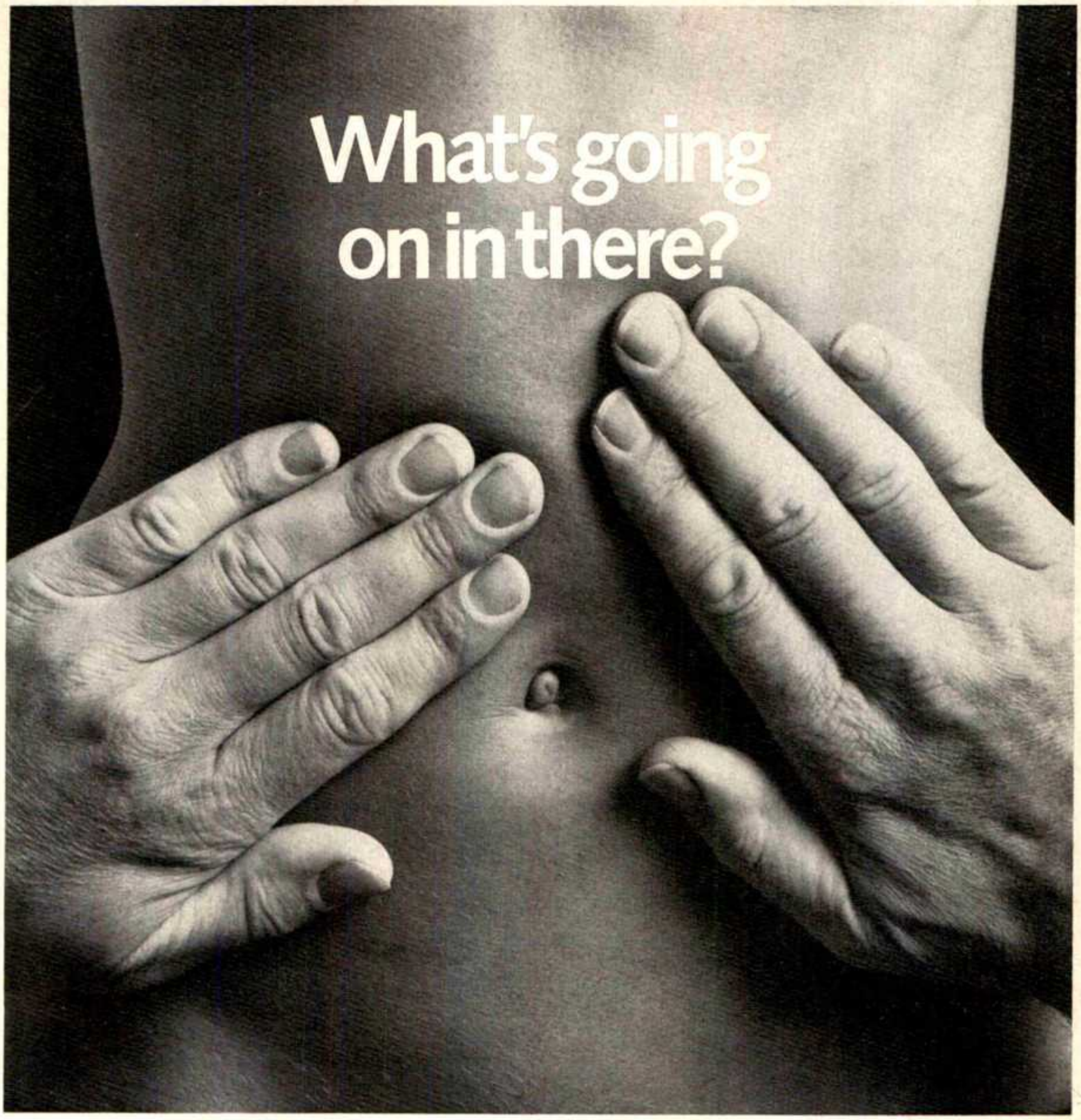
When it comes to rare-earth x-ray systems, here's only one which offers a fully comprehensive ange of screens and films, designed to outperform ll the others on the three most critical parameters f: diagnostic quality, radiation dosage and ong-term economy.

3M Trimax System. The most versatile, comprehensive and durable rare-earth system available. Specify it with confidence.

For further information about the Trimax System from 3M - the leaders in rare-earth phosphor technology - contact: Alan Budge, X-Ray Products, 3M United Kingdom Ltd, 3M House, PO Box 1, Bracknell, Berks, RG12 1JU. Telephone Bracknell (0344) 58458.

3M and Trimax are trade marks

3M



Trust baritop to tell you

Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.

for the treatment of malignant effusions

Coparvax is a freeze-dried preparation of Corynebacterium parvum. When injected into previously-aspirated pleural or peritoneal effusions, Coparvax has been shown to be extremely effective at preventing recurrence and easing the associated symptoms.

In addition, Coparvax has a remarkably low incidence of side-effects, unlike many other treatments, some of which may require concomitant narcotic analgesia.

For further information on this advance in the management of malignant effusions please contact our Scientific Services Division at the address below.

PRESCRIBING INFORMATION

Presentation Vial containing 7mg (dry weight of the inactivated *Corynebacterium parvum* organisms WFL strain CN 6134) with thiomersal, in a freeze-dried form. **Uses** Alleviation of malignant pleural effusions and malignant ascites. **Dosage** 7-14mg recommended, although some patients have responded to lower doses. **Administration** Freeze-dried Coparvax should be reconstituted with 1ml of physiological saline for injection and diluted in a further volume of 10-20ml prior to injection. The suspension should be injected, within 24 hours of reconstitution, into the pleural or peritoneal cavity via the paracentesis needle immediately after the effusion has been aspirated. Injection may be repeated, if necessary, at intervals of one to four weeks. **Contra-indications** During pregnancy, and patients with known hypersensitivity to thiomersal. **Precautions** The incidence and severity of side-effects attributable to Coparvax administered intrapleurally, appears to be intensified if given within 10 days of thoracotomy and lung resection, probably due to enhanced systemic absorption of Coparvax. Coparvax should not be given during the immediate post-operative period. Following intrapleural or intra-abdominal administration, leakage of Coparvax into subcutaneous tissues may result in local tenderness. Intense fibrinous reaction in the pleural and peritoneal cavities has been observed following local administration of Coparvax. Intestinal obstruction due to the formation of adhesions is a theoretical possibility, although it has not been reported as a complication of Coparvax administration. **Adverse effects** Fever occurs in 10 to 40% of patients following intracavitary injection. Abdominal pain or mild abdominal discomfort has been reported in some 20% of patients following intraperitoneal instillation. Nausea and vomiting may occur in a minority of patients following intracavitary administration of Coparvax. **Basic NHS Cost** Single vial (7mg), £30 (PL3/0097).

Coparvax*

Corynebacterium parvum

when the quality of life is the primary concern

Calmic Medical Division
The Wellcome Foundation Ltd.
Crewe, Cheshire
(Tel: 0270 583151)

*Trade Mark

SIEMENS
When programmed x-ray diagnosis is preferred, we have the ideal combination
SIREGRAPH-C
SIEMENS
Programme
Manual

The multipurpose Siregraph C automatic x-ray table has enhanced routine diagnostic capability, including aniography of the body trunk and lower extremities.

The escutcheon of the Tridoros 712 MP generator puts all the radiographic parameters at your fingertips by means of microprocessor technology.

Programmed radiographic factors may be inserted by the Superintendent Radiographer or Radiologist and these factors are retained permanently under lock and key. This 70kW 12 pulse machine maintains high voltage accuracy yet offers extreme flexibility with provision for 49 programmes each for radiography and planigraphy.

For full details contact: Siemens Medical Group,
Siemens Limited, Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS. Telephone: (09327) 85691.

Siemens–the ultimate in cost effective x-ray diagnosis

Now Available

a completely up-to-date and comprehensive text on the radiology of the brain and spinal cord . . .

Neuroradiology

Edmund H. Burrows and Norman E. Leeds

1981 2 volumes 944 pages
2845 half-tones and 76 line illustrations
hardback £95.00 ISBN 0 443 08016 X

This is a major new reference work for the practising radiologist. It is a practical, clinically-oriented text, with the emphasis on clinical diagnostic radiology, not on neuroradiological technique.

☐ one of the first textbooks of neuroradiology to include CAT scanning
☐ also includes information on the neuroradiological practice of the water soluble contrast agent metrizamide

The book is divided into two volumes:
VOLUME 1 is a textbook of Neuroradiology.
VOLUME 2 consists of 100 self-testing exercises.

If you would like more detailed information on this major new book, please write to:
Churchill Livingstone, Robert Stevenson House,
1-3 Baxter's Place, Leith Walk,
EDINBURGH EH1 3AF, U.K.

Churchill Livingstone
Robert Stevenson House, 1-3 Baxter's Place, Leith Walk, Edinburgh EH1 3AF, U.K.

X-ray equipment for sale from St. George's Hospital, London SW1

1 GEC Watson on track with Series II Diagnostic tube matchlet with tomographic attachment
2 Deans plain bucky table
3 Siemens simple bucky table
4 Philips Super 100 Generator and control unit
5 Siemens Heliophos 4E Generator
6 Watson R600 Generator
7 Philips Fluoroscopy table 90/90 complete with assorted attachments including serial device intensifier 9in CCTV with two monitors with Arriflex cine camera ceiling suspended Mullard tube
8 Watson Autonome 6 table
9 GEC Escort moving top bucky table with Kompact 9 image intensifier complete with GEC MX4 Self rectifying tube head CCTV and Monitor
10 Siemens Biangulix with 125/30/50R tube
11 A number of lead protection panels
12 Leadlined box
13 Kodak M 100 Processor

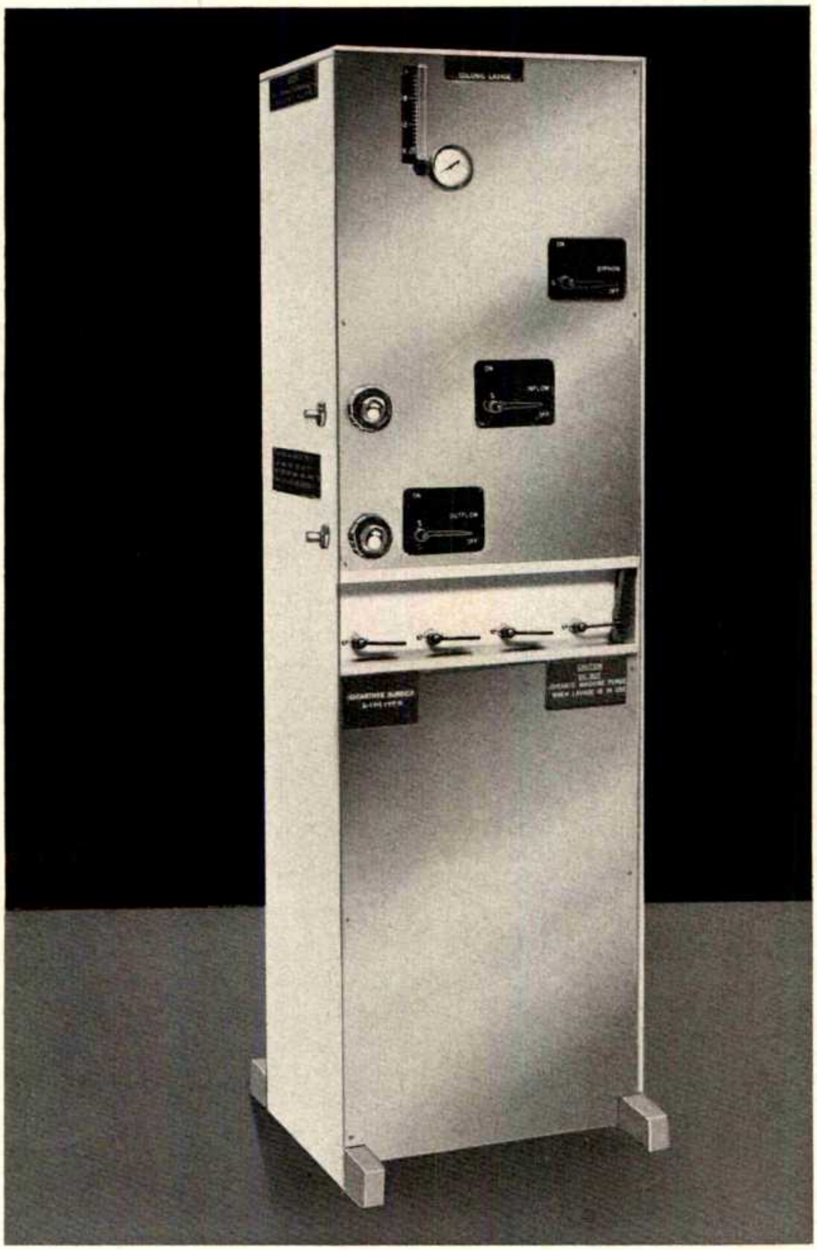
Other X-ray Equipment for Sale

14 GEC Deans 404 de luxe table 90°/30° Adverse tilt with Siemens Iontomat
15 CD40° dynamax 120 KVP tube stand
16 Philips, Free standing vertical bucky

This equipment is surplus to requirements and up to mid 1980 was serviced under maintenance contracts since then it has not been used.

To view please contact Mr Randall, 01–672 1255, ext 138. Offers in writing to Mr J. Gilder, District Supplies Officer, 72 St James' Drive, London SW17 7RS

HENDERSON
COLONIC LAVAGE UNIT



The Henderson Colonic Lavage provides a simple, effective and safe apparatus for washing out the large intestine and the terminal ileum of the small bowel.

The Henderson Colonic Lavage is indicated for patient preparation prior to surgery or radiography.

An important feature of this machine is, that as fluid is withdrawn from the patient, air is admitted to maintain the full lumen of the bowel, permitting complete fluid evacuation and assisting further faecal removal.

Macarthys Surgical Ltd

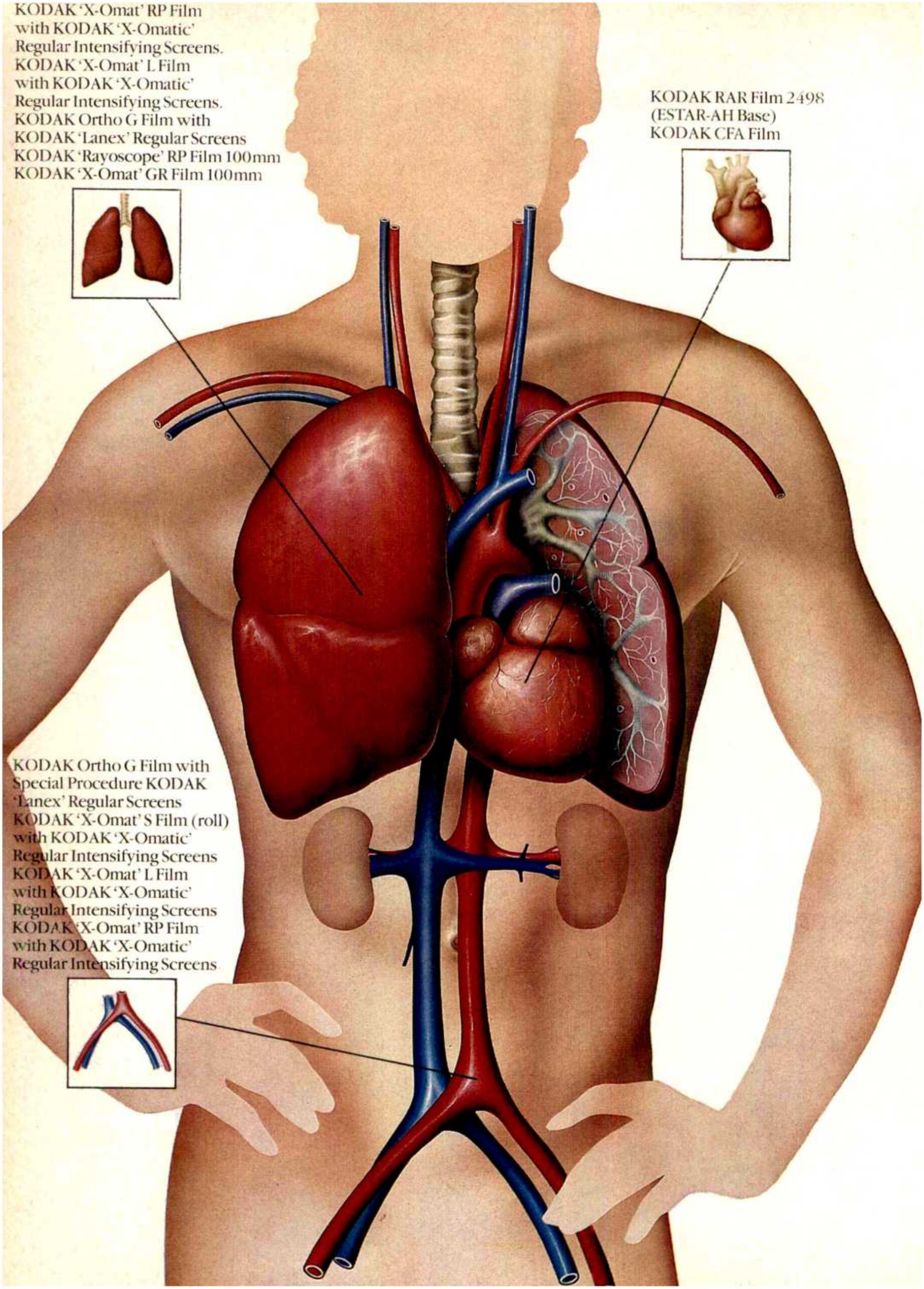
DAGENHAM
Selinas Lane
Dagenham, Essex RM8 1QD
Tel.: 01-593 7511

BIRMINGHAM
Unit 25/28
Edgebaston Shopping Centre
Hagley Road
Birmingham B16 8SH
Tel.: 021-454 6713

GLASGOW
301-3 Glentanar Road
Balmore Industrial Estate
Glasgow G22 7UG
Tel.: 041-336-8782

LIVERPOOL
201-3 London Road
Liverpool L3 8JS
Tel.: 051-207-1348

MANCHESTER
Precinct Centre
Oxford Road
Manchester M13 9GS
Tel.: 061-273-6754/5



KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK 'X-Omat' L Film
with KODAK 'X-Omatic'
Regular Intensifying Screens.
KODAK Ortho G Film with
KODAK 'Lanex' Regular Screens
KODAK 'Rayoscope' RP Film 100mm
KODAK 'X-Omat' GR Film 100mm

KODAK RAR Film 2498
(ESTAR-AH Base)
KODAK CFA Film

KODAK Ortho G Film with
Special Procedure KODAK
'Lanex' Regular Screens
KODAK 'X-Omat' S Film (roll)
with KODAK 'X-Omatic'
Regular Intensifying Screens
KODAK 'X-Omat' L Film
with KODAK 'X-Omatic'
Regular Intensifying Screens
KODAK 'X-Omat' RP Film
with KODAK 'X-Omatic'
Regular Intensifying Screens

An outline of Kodak products for cardio-vascular examination.

Kodak has the most comprehensive service network in the country.

We back that service with a range of products that includes over thirty diagnostic imaging films; and covers processors, cassettes, intensifying screens, chemicals and daylight handling equipment.

Kodak Service is there to help you maintain consistent image quality.

In the working environment, this means we can aid with planning an efficient process area.

In human terms, we can help with the training of radiologists, radiographers and technicians: on your premises or at our own Marketing Education Centre.

Equipment maintenance is also an important quality control factor, and Kodak provides a highly competitive service from strategically located Sales Centres.

For details, speak to your Kodak representative.

He can give you up-to-date information on all areas of diagnostic imaging.

Kodak. We care about your image.

KODAK 'Lanex' Regular Screens for special procedures are available to fit Puck, AOT and CGR rapid film changers. Kodak and all product names printed thus – 'X-Omat' – are trade marks.

Half page: 25×36 ems (Whole page: 51×36 ems)

Effective October 1, 1981

The British Journal of Radiology

The official organ of The British Institute of Radiology. Incorporated by Royal Charter

Rates for Advertisements

Page size	One Insertion £	Six Insertions £	Twelve Insertions £
Whole page (black & white)	128·00	120·00	113·00
Half page	74·00	70·00	64·00
Quarter page	40·00	38·00	36·00
Eighth page	28·00	27·00	25·00

Colour rates on application
Bound in advertisements £180
Loose advertisements £200
Box Number fee £5

Double page spread discount £10
Bleed page plus £25·00
Preferential positions (facing editorial/facing covers) plus 20%

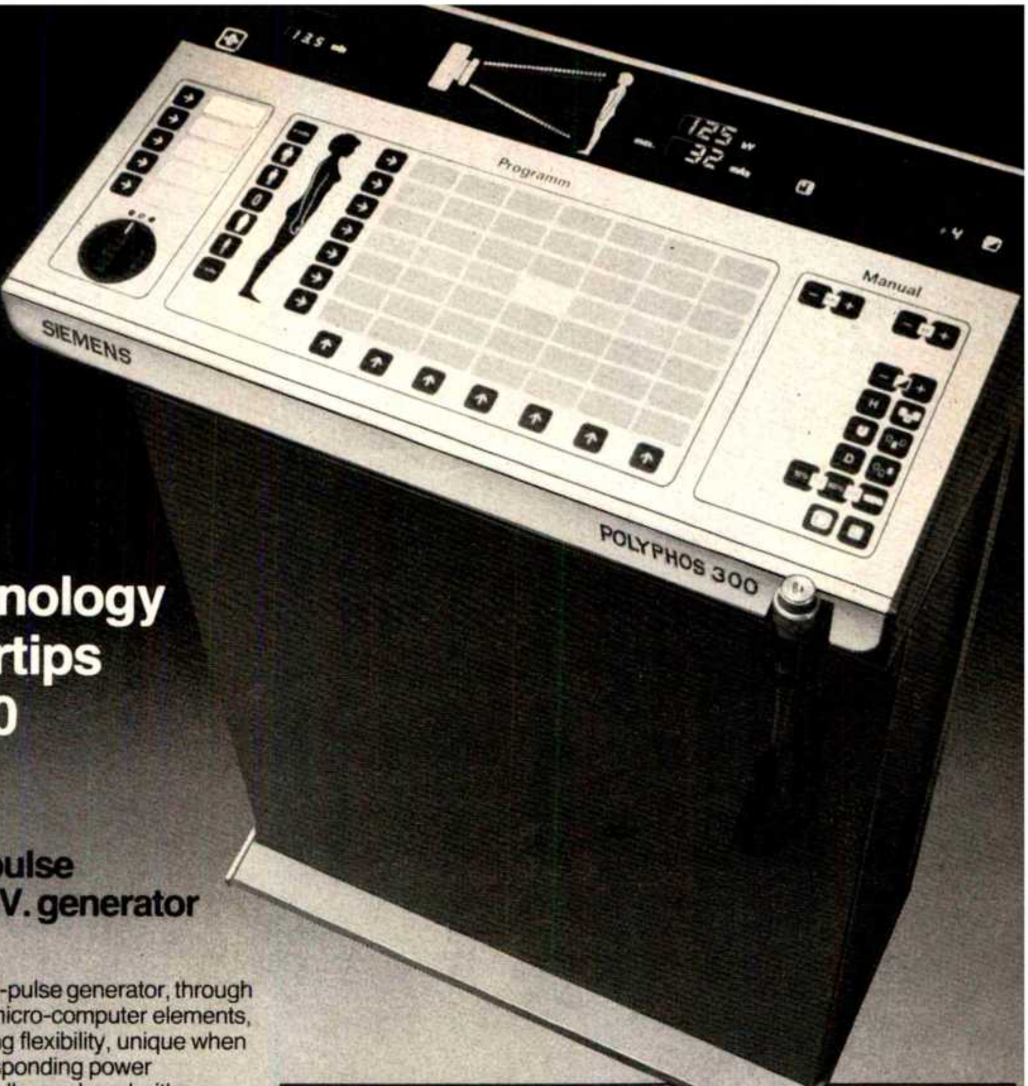
Terms: Monthly net. Series orders must be completed within a year. The right is reserved to decline or omit any advertisement. No responsibility can be accepted for the omission to insert an advertisement from any cause.
Copy must be received 6 weeks preceding the publication date, and no alterations or corrections can be made unless the amended proofs are returned before noon on the 1st of the month

All applications for space to be made to
Advertising Department
British Journal of Radiology
24a Litchfield Street, London WC2H 9NX. Tel. 01–836 5281

Eighth page: 12×17½ ems

Quarter page: 25×17½ ems

SIEMENS



Flexible technology at your fingertips Polyphos 300

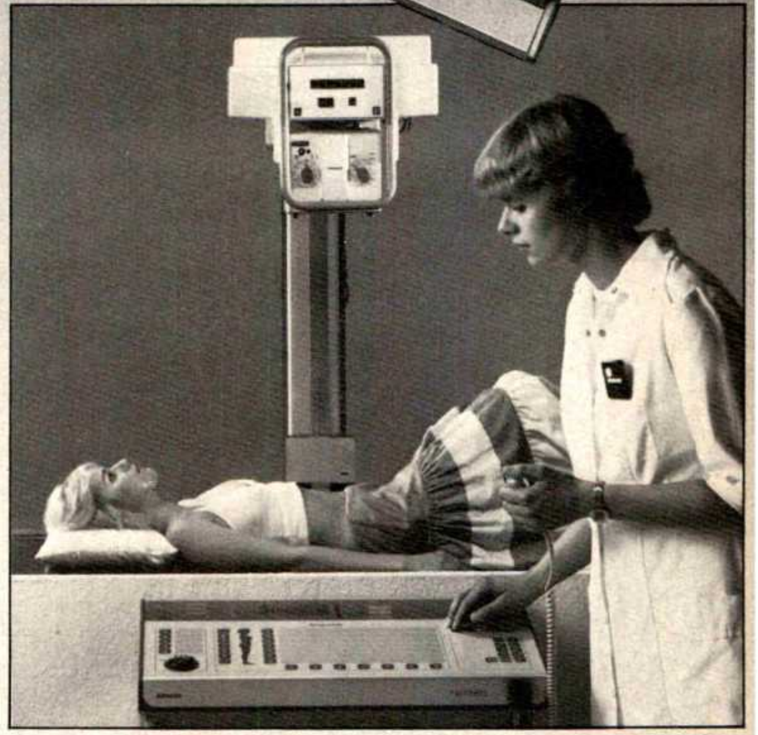
Single-tank multi-pulse diagnostic X-ray H.V. generator – 30KW

The POLYPHOS 300 multi-pulse generator, through the utilisation of ultra-modern micro-computer elements, offers a high degree of operating flexibility, unique when compared with units of a corresponding power classification. It can be universally employed with diagnostic X-ray examination units for radiography, fluoroscopy or planigraphy.

The multiprogramming system (organ related exposure technique) enables any freely selectable exposure parameter to be incorporated into an organ-related program, by the operation of a single button.

Features include:

- ❇ Highly compact design, requiring minimum installation area.
- ❇ Single-tube unit utilizing medium frequency converter technology.
- ❇ Rapid high-voltage and tube current regulation during exposure.
- ❇ Short exposure times.
- ❇ Continuously falling load.
- ❇ Up-to-the-minute technology, with micro-computer elements.
- ❇ Smooth control panel with touch buttons.
- ❇ Flexible extension system.
- ❇ High dose yield as a result of the multipulse configuration.



For full details contact: Siemens Medical Division,
Siemens Limited, Siemens House, Windmill Road,
Sunbury-on-Thames, Middlesex TW16 7HS.
Tel: Sunbury-on-Thames (09327) 85691.
Telex: 8951091.

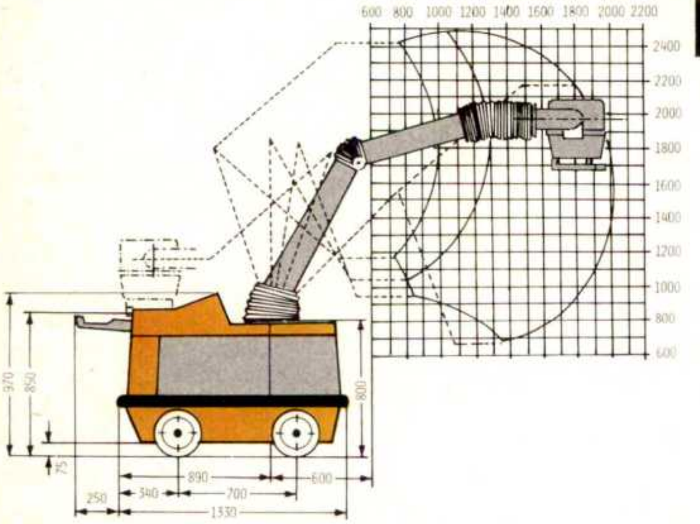
Siemens – X-ray innovation is our business

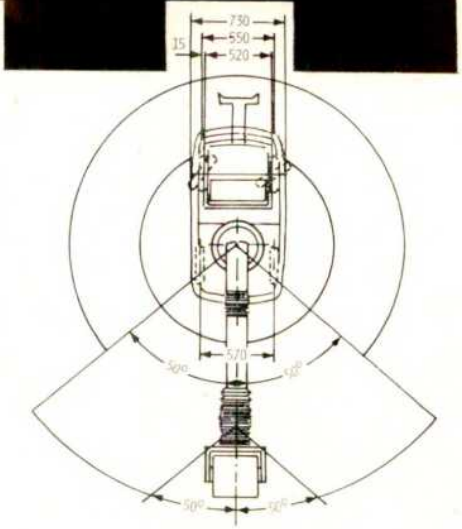
SIEMENS

Mobil XR – brings a microprocessor controlled, aseptic mobile radiography unit to the patient.

The battery-powered MOBIL XR is self-propelled and self-contained with microprocessor controls providing full power exposures at 20 kW time after time. The adjustable counter-balance arm and a wide range of alphanumerically displayed exposure parameters allow sharp image examination of any organ or limb. Aseptic design with touch controls and total enclosure fo all components make it ideal for theatre use. Infinitely variable speed control makes it easy to manoeuvre and pull-out cable allows simple recharging at any power point.

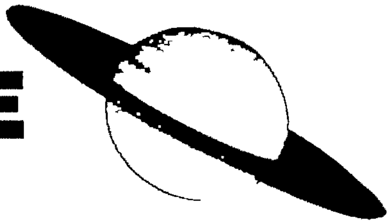
For further details or a demonstration contact:
Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS.
Tel. Sunbury (09327) 85691.

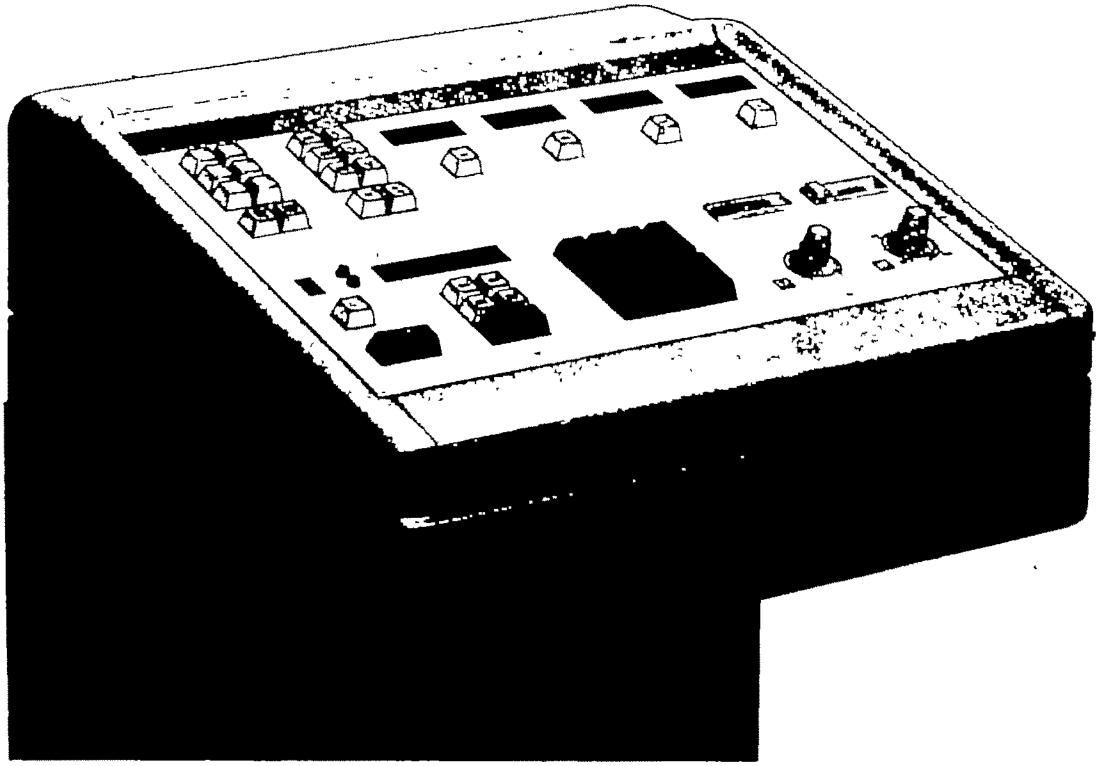




In the world of mobile radiography Siemens has the answer.

THE COMPUTERIZED GENERATOR OF TOMORROW IS HERE TODAY





SATURN– THE MICROPROCESSOR CONTROLLED GENERATOR

FLEXIBILITY
- One, two or three factor control
- Operator input to memory store
- Over 200 operator introduced programmes
- Last exposure on each auxiliary memorised for instant recall

DIGITALLY DISPLAYED
- kV mA mAs time
- Post exposure of mAs and time
- Organ and projection
- Number of further exposures possible
- Diagnosed error or malfunction

PHILIPS

PHILIPS Medical Systems

For detailed information write to Philips Medical Systems, Kelvin House, 63/75 Glenthorne Road,

Computerized Tomographic Scanners in Radiotherapy in Europe

Edited by Roger J. Berry

British Institute of Radiology
Supplement 15

Under the auspices of the Commission Informatique of the European Association of Radiology, a Workshop was held at the Headquarters of WHO, Geneva, from 28 to 30 March 1979 on 'The Use of Computerized Tomographic Scanners in Radiotherapy in Europe'. It was clear from the first that CT scanning would have a major impact on radiotherapy, but how and where? At this meeting 150 experts from 17 countries met to review, from a real background in clinical experience of using CT scanners in radiotherapy planning, the progress which had been made and the costs involved. CT scanning is not inexpensive, but the information provided is in many cases unique. Following a keynote address by Professor Brian Pullan of the University of Manchester outlining what is and is not likely to be possible in future in tumour imaging, the papers cover the practical use of CT scan information in assessing tumour volume, planning radiotherapy and following tumour response in the head and neck, the thorax and the abdomen. The linkage of CT information to radiotherapy treatment planning is discussed, and the way indicated towards true three-dimensional radiotherapy planning. All the papers presented at the Meeting are included in abridged form as well as rapporteurs' reports of the discussions in each section.

Price £19·50
ISBN 0 905749 09 X
ISSN 0007 1285

Orders to:
Publications,
The British Institute of Radiology,
36 Portland Place,
London W1N 3DG
or your local bookseller.

Diagnostic Radiologist

Diagnostic Radiologist wanted, with fellowship or eligible, to join radiological group in Edmonton, Alberta, Canada. Hospital and office practice. Applicant should have training in special procedures and/or ultrasound.

Please reply to:
Dr. W. J. Taylor, M.B., Ch.B., D.M.R.,
F.R.C.A.(C.)
#360 10830-Jasper Avenue
Edmonton, Alberta
Canada T5J 2B3

JEDDAH
SAUDI ARABIA

RADIOLOGIST– C.T. SCANNER SPECIALIST

The New Jeddah Clinic, a private hospital, urgently requires a Radiologist with at least three years' experience in C.T. Scanning.
Excellent salary and benefits.

For further information please contact:
Remedy International,
70 Old Brompton Road,
London SW7 3LQ Tel: 589–6658

ST MARK'S HOSPITAL
DAY COURSE

TUESDAY NOVEMBER 10th 1981

Real Time Ultrasonography

and

Inflammatory Bowel Disease Colorectal Cancer

Closed Circuit TV Demonstration Lectures

Fee £12 including lunch and refreshments

For further details write to:
The Secretary
Department of Postgraduate Studies
St. Mark's Hospital
City Road
London EC1V 2PS

Automatic, Computer-controlled Dynamic and High Resolution Static B-scanning

The Sonography System RA-1 diagnostic ultra-sound scanner uses sophisticated, computer-controlled image processing to achieve superior image resolution. The advanced, state-of-the-art scanheads comprise:

- LFOV scanheads for multiformat abdominal scanning.
- WV scanheads for high frame-rate scanning.
- Small parts scanhead, incorporating Doppler with Spectral Analysis, for superficial vessel and organ studies, for neonatal and paediatric scanning.

The modular design guards against obsolescence whilst permitting expansion and the ability to retrofit new imaging techniques as they are developed.

Universal Computer-controlled High Resolution Static B-scanning

The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

- Wide range of transducers
- Image Process Functions
- Area, Circumference and Volume measurements.
- Obstetrics measurement facility
- Floppy disc interface

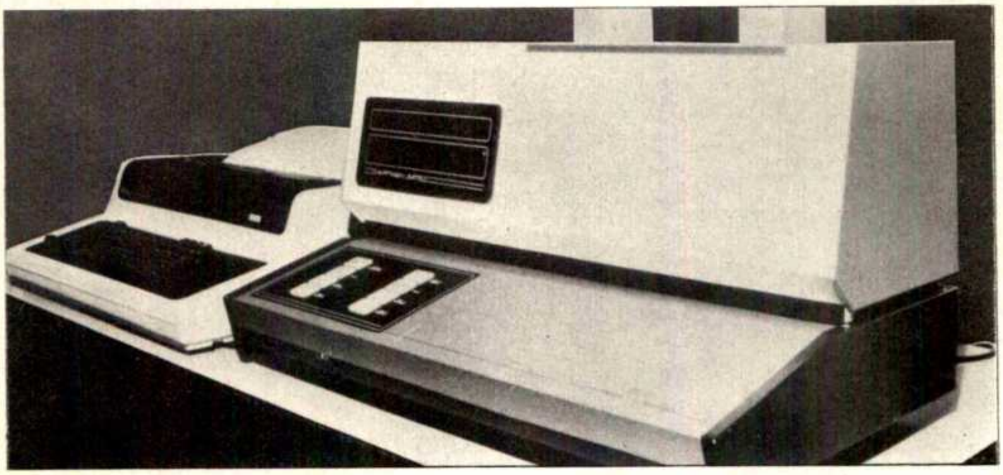
Future improvements to the image processing may be incorporated due to the flexible computer software.

Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner.
For full details write to: Siemens Medical Group, Siemens Limited, Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691.

...Siemens gives you the choice!

Pitman's revolutionary new Series '800' range of Thermoluminescence Dosimetry Processors

Since D. A. Pitman Limited pioneered TLD over 15 years ago, they have designed and produced a succession of processors that are renowned throughout the world and set the standards for all other readers. The Series '800' is no exception.

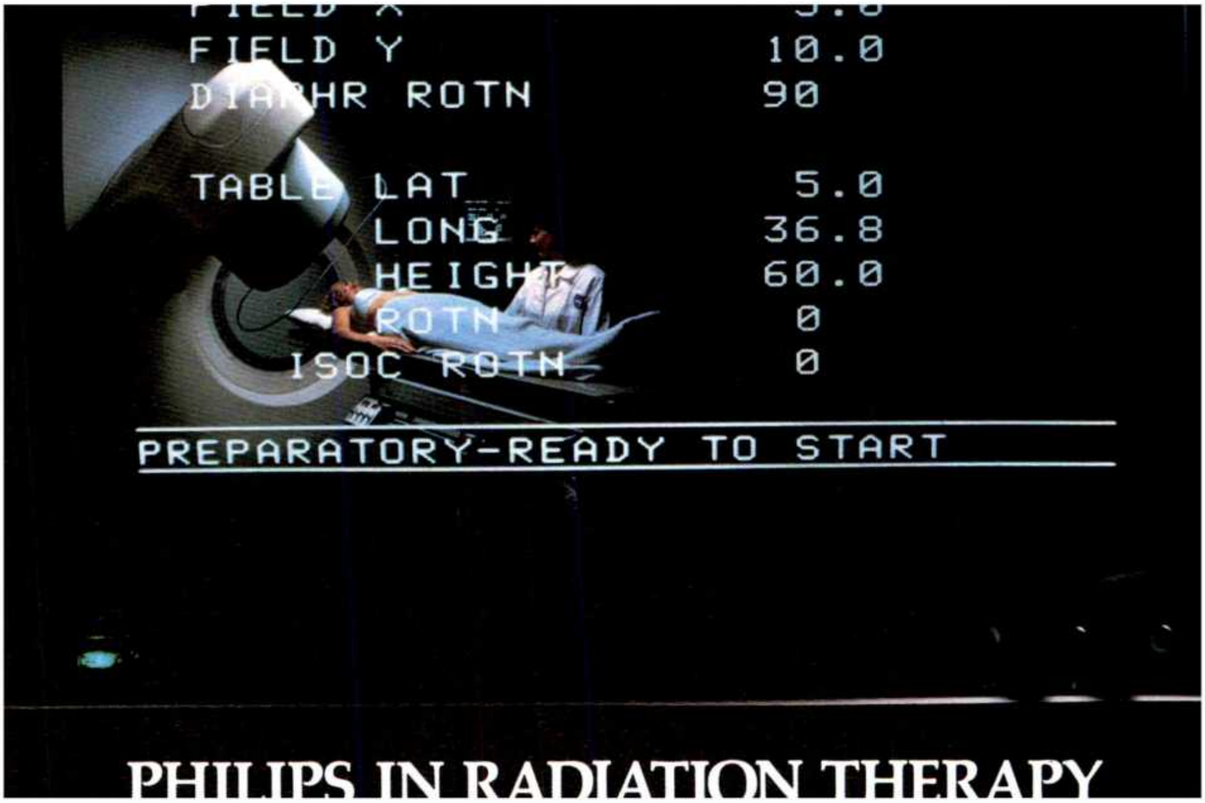


Model 806 Automatic TLD Processor

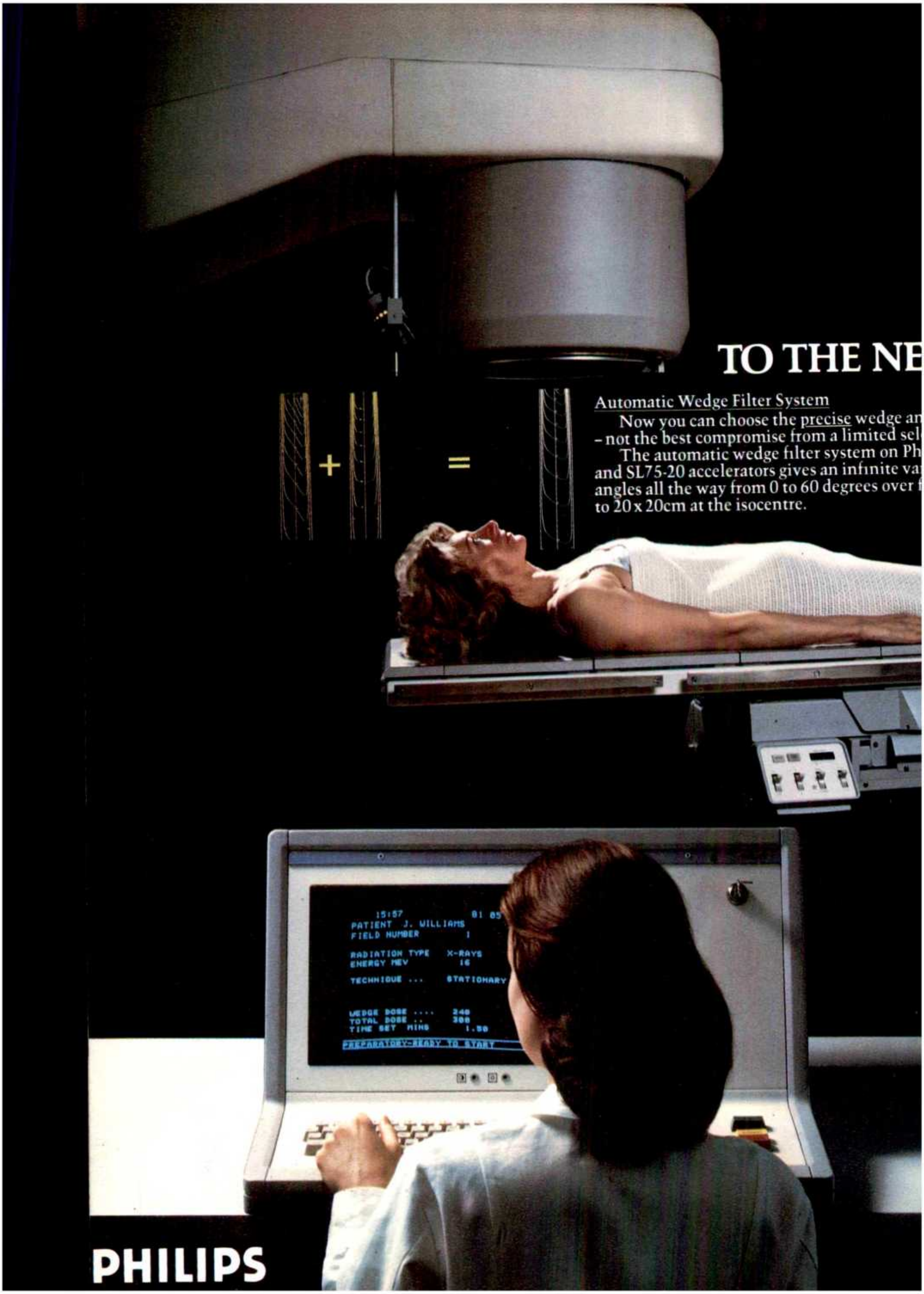
- Designed specifically for personnel monitoring
- Very simple operation by microprocessor control
- Tissue equivalent 2, 3 or 4-element dosemeters
- High sensitivity (2mr)/non light affected PTFE/LiF or pure LiF disk dosemeters
- Choice of badges with filtration complying with international standards.
- Advanced precision thermal contact heating system for reproducible results and fast (10s) readout
- Fully automatic readout of re-usable dosemeters
- Computer compatible input and output
- Comprehensive range of ancillaries and variants

For full details, please contact:

D.A. Pitman Ltd (Dept. AD 237) Jessamy Road, Weybridge, Surrey KT13 8LE
Telephone Weybridge (0932) 55721 Telex 929823



PHILIPS IN RADIATION THERAPY



```
      15:57                  01 05
   PATIENT  J. WILLIAMS
   FIELD NUMBER              1

   RADIATION TYPE   X-RAYS
   ENERGY MEV         16

   TECHNIQUE ...    STATIONARY


   WEDGE DOSE ....   240
   TOTAL DOSE ..     300
   TIME SET  MINS      1.50
 PREPARATORY-READY TO START
```

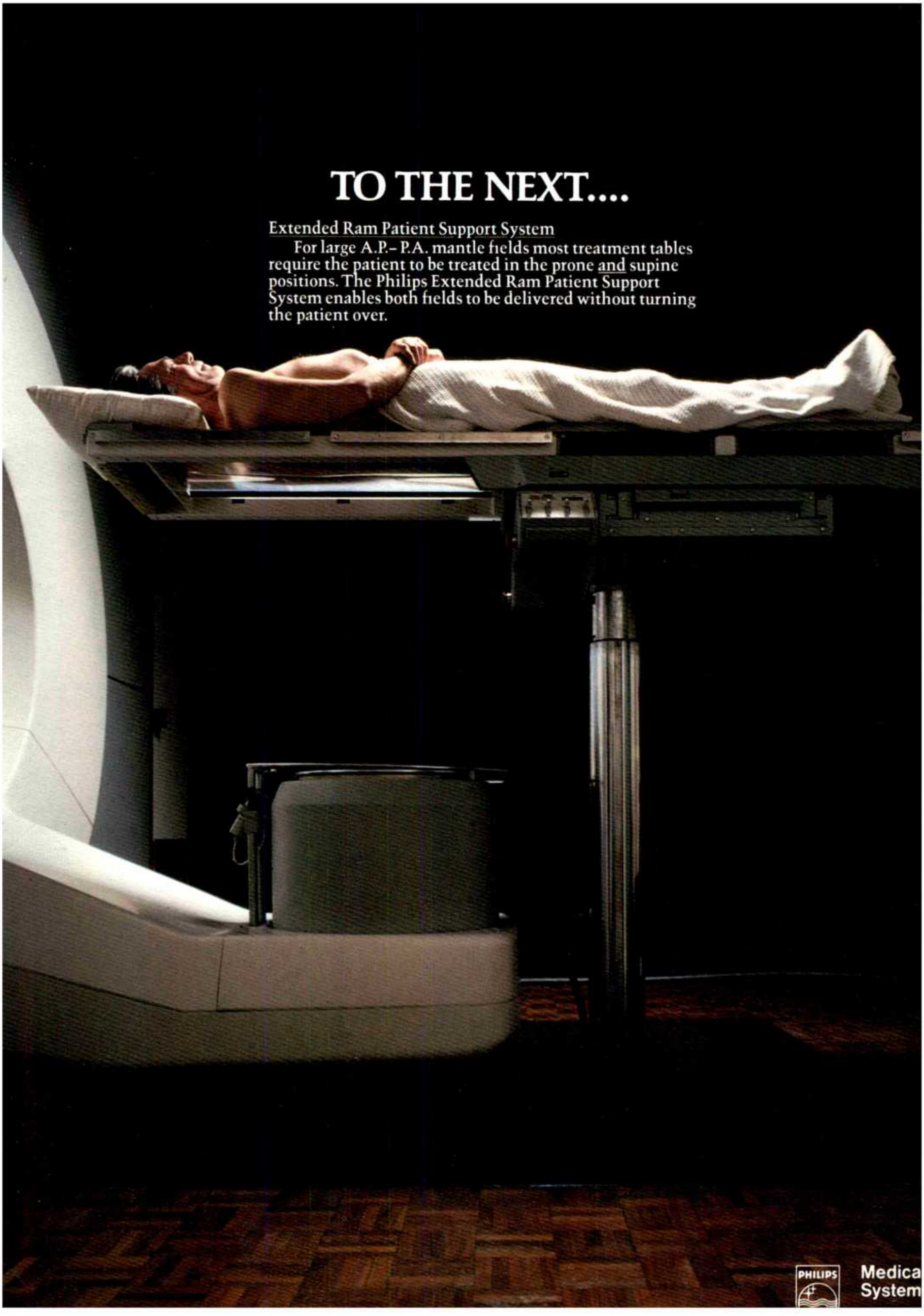
TO THE NE

Automatic Wedge Filter System

Now you can choose the precise wedge an
– not the best compromise from a limited sel

The automatic wedge filter system on Ph
and SL75-20 accelerators gives an infinite va
angles all the way from 0 to 60 degrees over
to 20 x 20cm at the isocentre.

PHILIPS



TO THE NEXT....

Extended Ram Patient Support System

For large A.P.– P.A. mantle fields most treatment tables require the patient to be treated in the prone and supine positions. The Philips Extended Ram Patient Support System enables both fields to be delivered without turning the patient over.

PHILIPS

Medica
System

TO THE NEXT....

A complete electron therapy system

Motorized variable field applicators, Fixed circular square and rectangular applicators; Removable end frames for irregular field shapes; Interlocks and touch guards for added safety.

Microprocessor based treatment control consoles; Computerised Verification and recording systems;

Philips Linear Accelerators Simply Years Ahead.

Contact Philips at one of the addresses shown below
for more information on our full range of equipment for radiation therapy.

Philips Medical Systems, Kelvin House, 63/67 Glenthorne Road, Hammersmith, London W6 0LJ.
M.E.L. Manor Royal, Crawley, Sussex RH10 2PZ.
Divisions of Philips Electronic & Associated Industries Ltd.
Philips Medical Systems Inc, 710 Bridgeport Avenue, Shelton, Connecticut 06484, United States of America.
N.V. Philips, Medical Systems Division, Eindhoven, The Netherlands.

HILIPS

PHILIPS Medical Systems

SHIMADZU MEETS CUSTOMER DEMANDS
THROUGH INNOVATIVE ENGINEERING
MOBILE X-RAY
IMAGE INTENSIFIER
WHA-10

High quality image ....
- 0.4mm focus x-ray tube
- Image Brightness Stabilizer

High output ....
- Square full-wave rectification x-ray generator

Less x-ray radiation ....
- Video memory
- Motor driven collimator

Simple operation ....
- Radiographic condition memory (Optional)

Free access to patient ....
- Large C-arm steering handle

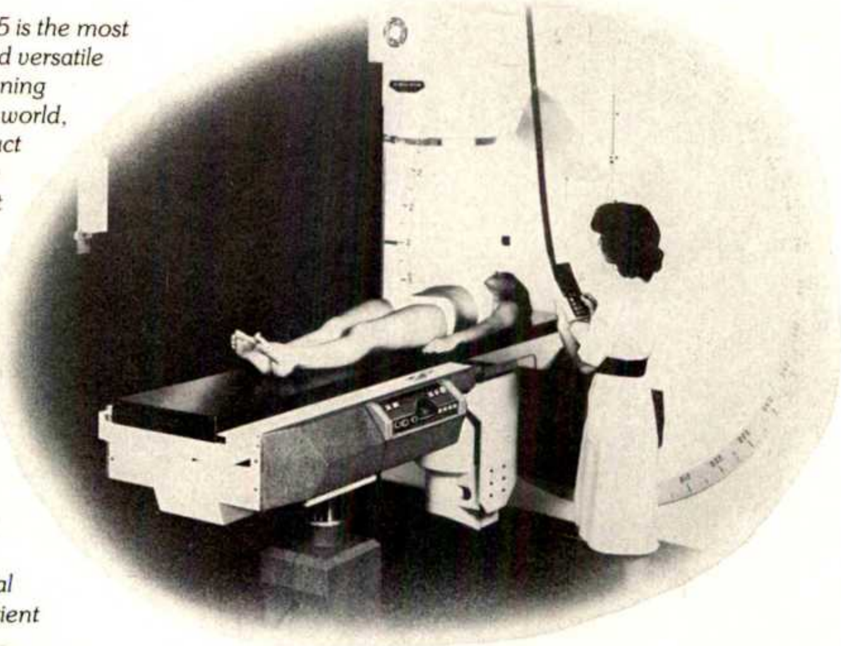
SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Dusseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D.
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

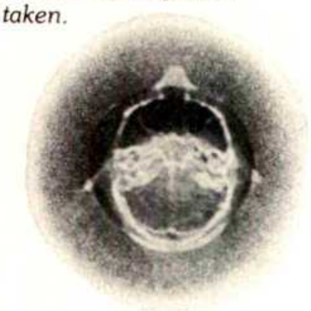
TEM

Ximatron 5
Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

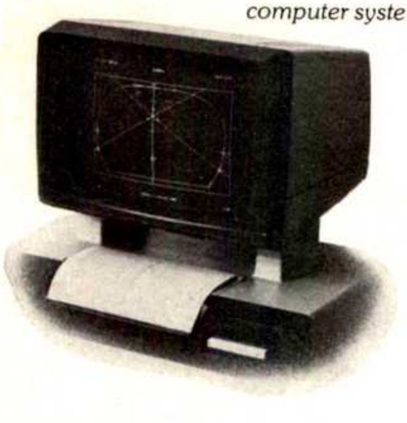


Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



For further details:

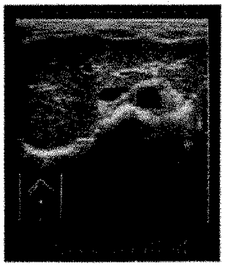
TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY

When you need to know the inside story,

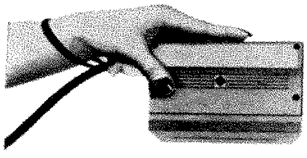
the Hitachi EUB-22 is a must.

More accurate clinical information is now available faster, thanks to Hitachi technology in this new real time ultrasound system.

The compact lightweight transducer provides access to all areas of interest making the TOMOSONIC EUB-22 ideal for abdominal, obstetric and neonatal imaging.

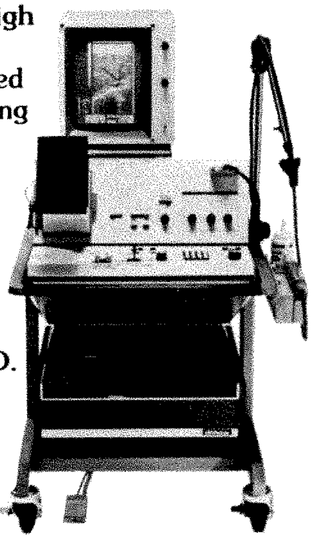


Dual image display allows expanded field of view or display of side-by-side images either in real time or freeze frame modes, with on-screen measurements.



Superb noise-free, high resolution images produced by advanced digital scan processing and transducer focussing techniques are displayed on the TV monitors. To facilitate the evaluation of those images the TOMOSONIC system provides an exclusive graphics display.

The patient's position during imaging is clearly displayed along with such valuable information as transducer position, patient I.D. date and gain.



SONOTRON MEDICAL ELECTRONICS

SONOTRON LIMITED 29 MIDLAND ROAD, BEDFORD MK40 1PL ENGLAND TELEPHONE: BEDFORD (0234) 40881

also in: AUSTRIA-(02236) 86945 BELGIUM-(02) 7213424 GERMANY-(098) 3205051 FRANCE-(06) 9286945 SWEDEN-(040) 77585
or contact EUROPEAN HEADQUARTERS: SONOTRON AG NEUGASSE 247 P.O. BOX 353 CH 8031 ZURICH, SWITZERLAND TEL: 41-1-425841

Research & development

GUERBET

Better contrast media through research

Laboratoire GUERBET
16-24, rue Jean Chaptal - 93601 Aulnay-sous-Bois - Cedex FRANCE
Tél.: 866.78.37 - Télex: 212382 F.

1981, *British Journal of Radiology*, *54*, 719–730

VOLUME 54 NUMBER 645 SEPTEMBER 1981

The British Journal of Radiology

A reappraisal of the genetic consequences of diagnostic radiology in Great Britain

By B. F. Wall, B.Sc., S. Rae, F.R.C.P., F.F.C.M., S. C. Darby, Ph.D. and G. M. Kendall, Ph.D.

National Radiological Protection Board, Chilton, Oxon

(*Received March 1981*)

ABSTRACT

The National Radiological Protection Board has recently carried out a reappraisal of the annual genetically significant dose (GSD) to the population of Great Britain arising from the practice of diagnostic radiology. The current value of 120 μGy (12 mrad) is indistinguishable from the value determined 20 years ago despite a 48% increase in the number of X-ray examinations performed per head of the population. This is mostly due to a large decrease in the contribution from obstetric radiology and to a marked reduction in the gonadal doses delivered to children for nearly all types of examination. The GSD and the frequency of X-ray examinations in Great Britain would appear to be considerably lower than those found in other industrialized countries and seem unlikely to result in more than 100 cases of serious hereditary ill-health per year at genetic equilibrium. On the other hand, diagnostic radiology is responsible for 87% of the GSD from all man-made sources of population exposure in Great Britain and there is evidence from the data collected for this reappraisal that radiological protection measures could be improved so as to reduce significantly this large contribution without detriment to patient care.

An assessment of the risks to the population and to future generations resulting from the use of ionizing radiation for medical purposes has not been carried out on a national scale in Britain for over 20 years. In 1960 a committee under the chairmanship of Lord Adrian reported on the annual genetically significant dose (GSD) to the population for both diagnostic and therapeutic uses of radiation and four years later they published an estimate for the mean *per caput* bone marrow dose arising from the same source. As far as the GSD was concerned they concluded that their estimate of 193 μGy (19.3 mrad) did not indicate any need for major restrictions in radiological practice and that the number and type of examinations or treatments should be dictated solely by the clinical needs of the patient. However, they were convinced that in many instances gonadal doses could be substantially reduced without detriment to the efficacy of the examination or treatment and recommended techniques for bringing this about. They also recommended that the situation should be kept under effective review.

In the ensuing 20 years considerable changes have taken place in the extent and techniques of medical radiology as well as in the appreciation of radiation risks. The small individual risk experienced by a patient during an X-ray examination should, of course, be justified by an overriding benefit resulting from more accurate diagnosis. The genetic risks, on the other hand, cannot be so readily dismissed as there is rarely any direct benefit to the descendants of the patient against which to offset the increased chance of inherited ill health, however small this may be. Furthermore, there is no opportunity for consulting those who may experience the genetic consequences. It is therefore incumbent upon national bodies like the NRPB, who are responsible for maintaining a watch on the hazards to the population from all sources of ionizing radiation, to determine the current level of the genetic consequences from medical radiology and to advise the appropriate authorities if it appears that an unacceptably high burden is being passed on to future generations. This responsibility is reiterated in a directive of the Council of the European Communities (CEC, 1976) which requires all member states to consider the radiation-induced genetic burden on society and to determine the magnitude of its components from different sources, particularly medical, in their own countries. The emphasis on medical radiology is due to the fact that in developed countries the use of ionizing radiation in health care provides the largest man-made component of the total collective population dose. A recent NRPB report (Taylor and Webb, 1978) indicated that it could contribute as much as 85% of the GSD to the population of the UK from all sources, barring natural background radiation.

Since diagnostic X-ray examinations involve far more of the fertile population than either radiotherapy or the use of radiopharmaceuticals, a reappraisal of the genetic consequences from this branch of medical radiology has been given priority. The results and implications of this reappraisal are summarized in the following sections of this report after a brief description of the survey techniques. More comprehensive technical details can be found in NRPB Reports R104, R105 and R106 (Kendall *et al.*, 1980; Wall *et al.*, 1980; Darby *et al.*, 1980). Meanwhile the contributions from radiotherapy and nuclear medicine are currently being assessed together with methods for quantifying the somatic risks to patients, and will be published in due course.

Method of Reappraisal of Genetic Consequences

In line with the majority of previous national surveys and following the recommendations of UNSCEAR (1972; 1977), the quantity "Genetically Significant Dose" (GSD) has been used to indicate the relative amount of genetic injury to be expected from the non-uniform irradiation of a large number of people. The GSD is defined as that dose which, if given to every member of a population, would produce the same total genetic injury as the actual doses received by the various individuals (UNSCEAR, 1972, p. 134).

The total genetic injury to the population is taken to be

$$\Sigma a P_i D_i = a \Sigma P_i D_i \quad . \quad . \quad . \quad (1)$$

where P_i is the child expectancy of the i^{th} individual; D_i is the gonadal dose to the i^{th} individual; a is a constant of proportionality and summation is over every individual in the population.

From the definition of GSD, if all individuals in the population received exactly the GSD, then the total genetic injury would be the same as that resulting from the actual doses received. Thus

$$a \Sigma P_i \, \mathrm{GSD} = a \Sigma P_i D_i$$

Hence

$$\mathrm{GSD} = \Sigma P_i D_i / \Sigma P_i \quad . \quad . \quad . \quad (2)$$

When considering the annual GSD from diagnostic radiology it is convenient to group the population by age and sex and then within each age–sex group to consider the number of individuals who underwent each of the various examination types. The GSD can then be written in the following form

$$\mathrm{GSD} = \Sigma_{kl} E_{kl} \bar{D}_{kl} / \Sigma_k E_k$$

where E_{kl} is the total number of future children expected by those in age–sex group k undergoing examinations of type l in a year; $\bar{D}_{kl}$ is the mean gonadal dose received by an individual in age–sex group k who underwent an examination of type l; E_k is the total number of future children expected by those in age–sex group k.

Estimates were therefore required of the number of people in each age–sex group examined annually in Great Britain, broken down by examination type, the child expectancy of these people and the average gonadal dose delivered by each type of examination.

Information on the frequency of X-ray examinations was obtained by sending questionnaires to a sample of about 100 hospitals throughout Great Britain. In England and Scotland, hospitals were selected by a stratified sampling procedure based on the workload of their X-ray departments. In Wales, hospitals were selected using an informal procedure. The questionnaires asked for details of every X-ray examination carried out in a specified week in June 1977. These included the sex and age of the patients and the type of examination, as well as technical factors such as the number of films, the fluoroscopic screening time, and the use of gonadal shielding. Sufficient hospitals responded to achieve a standard error of 5% in the estimated total of examinations for the whole country. Annual totals were estimated by multiplying the weekly figures by 365/7 and then correcting for seasonal variations in workload based on film consumption data for Britain in 1977.

Estimates of the child expectancy of the population were obtained from the work of Taylor (1980) based on official statistics provided by the Office of Population Censuses and Surveys.

Gonadal doses were measured directly on patients undergoing 13 selected types of diagnostic examination at 21 hospitals. Thermoluminescent dosemeters were used which consisted of lithium borate powder contained in adhesive polythene sachets. For male patients they were attached to the inside of the thigh close to the scrotum and were assumed to receive the same dose as the testes. For female patients they were positioned so as to measure the entrance skin dose level with the ovaries. Skin doses were converted to ovarian doses using factors obtained by exposing an anthropomorphic phantom to a range of typical diagnostic X-ray fields and measuring the doses at the ovary sites and on the skin. The 13 examination types selected for inclusion in the dose-measurement survey were those that in previous surveys accounted for about 95% of the GSD. Doses for all other examination types were obtained from the current literature. The 21 hospitals visited came from all regions of the country and included a representative sample of X-ray departments taking account of size and speciality. At the end of the survey the gonadal doses received by 4565 patients had been measured.

RESULTS OF THE REAPPRAISAL

1. *The current extent of X-ray diagnostic radiology*

The frequency survey indicated that 21.3 million X-ray examinations were carried out in National Health Service (NHS) hospitals in Great Britain in 1977. This represents an increase of 64% over the estimate of 13 million from the 1957 national survey (Adrian, 1960). As the population has grown during the intervening period, the number of examinations per thousand of the population has risen by 48%, which corresponds to an increase of 2.0% per annum.

Estimates were made of the numbers of examinations conducted outside NHS hospitals and these are shown in Table I with the corresponding figures from the Adrian survey. These bring the total number of examinations (excluding dental radiology) up to 23.8 million, amounting to 440 examinations per thousand of the population in 1977.

In addition to medical radiology, about 5.8 million dental examinations were carried out amounting to about 110 examinations per thousand of the population. This is an increase by a factor of nearly six since 1957. A detailed analysis of the growth in dental radiology has been published by Kendall *et al.* (1981).

The survey has also demonstrated an increase in complexity of many diagnostic X-ray examinations in recent years. The mean number of films per examination has increased from 1.9 in 1957 to 2.4 in 1977. Those examinations which showed a particularly large increase in film usage were angiographic examinations of the head and abdomen and barium contrast studies of the gastrointestinal tract.

The relative frequencies of the more common types of examination carried out in NHS hospitals are shown in Fig. 1. Not surprisingly X-rays of the chest, limbs and extremities are predominant. However, chest radiography has fallen from 48% of all examinations in 1957 to 33% in 1977, presumably reflecting the progress which has been made in controlling tuberculosis. About 4% of these chest radiographs employed mass-miniature photofluorographic techniques rather than full-size radiography. A number of mass-miniature chest X-ray units are still operating outside NHS hospitals but, as Table I shows, the number of examinations that they performed has dropped by a factor of over three since 1957. Some of the less common examinations have also shown some interesting trends. For example, the number of obstetric examinations per thousand live births has fallen from 114 in 1957 to 42 in 1977, no doubt as a consequence of the increased concern for possible fetal damage and the extensive use of ultrasound as an alternative to X rays. There has also been a drop in the number of cerebral angiograms as a result of the advent of computerized tomography. Most other types of radiological examinations have increased in frequency. The largest increase was seen in radiography of the pelvis and in cystography, both of which are about five times more frequent now than they were in 1957.

About 6% of all radiological examinations reported in the current survey involved fluoroscopy.

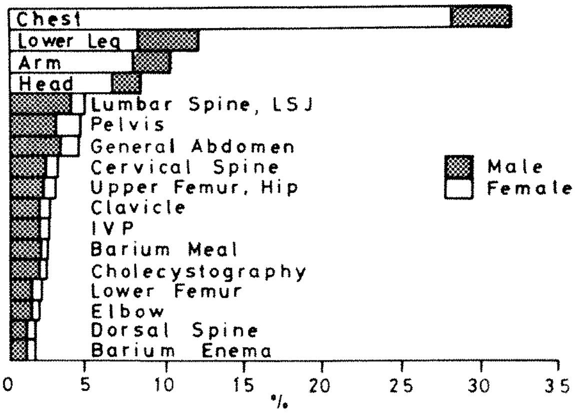


FIG. 1.

Relative frequency of examinations in NHS hospitals. For each type of examination the horizontal bars representing the relative frequency for each sex are superimposed so that the longer one only appears beyond the right hand limit of the shorter one.

TABLE I

ESTIMATED ANNUAL FREQUENCIES OF X-RAY EXAMINATIONS FROM DIFFERENT SOURCES IN 1957 AND 1977

Source	Number of examinations × 10^6	
	1957	1977
NHS hospitals	13	21.3
Mass miniature chest X rays	4.77	1.40
Armed forces	0.412	0.418
Private hospitals	0.286	0.323
Private practice	0.100	0.250
Other (e.g. occupational)	0.288	0.135
Total (excluding dental)	18.8	23.8
Dental radiography	1.00	5.75
Total	19.8	29.6

TABLE II

MEAN GONADAL DOSES MEASURED IN THE CURRENT SURVEY BY EXAMINATION TYPE, AGE GROUP AND SEX

	Mean gonadal dose (mGy)							
	Male				Female			
Examination	All	0–15	16–45	>45	All	0–15	16–45	>45
Lumbar spine, LSJ	0.58	0.42	0.64	0.52	3.80	1.94	3.90	3.84
Upper femur, hip	6.38	1.62	6.13	10.5	0.75	0.16	0.96	1.03
Pelvis	5.53	1.46	2.94	7.62	1.64	0.33	1.16	2.21
Intravenous pyelography	3.87	0.60	3.57	4.67	3.24	1.64	3.11	4.02
Cystography	4.50	2.53	18.0	18.0	6.30	4.29	14.0	14.0
Abdomen	1.51	0.66	1.58	1.67	0.80	0.51	0.79	0.85
Barium enema	3.30	1.38	2.50	3.57	15.9	4.54	14.3	16.6
Obstetric abdomen	Fetal	Gonad	Dose =	3.40	3.10	—	3.10	—
Barium meal	0.28	0.12	0.27	0.32	2.82	0.17	1.54	5.01

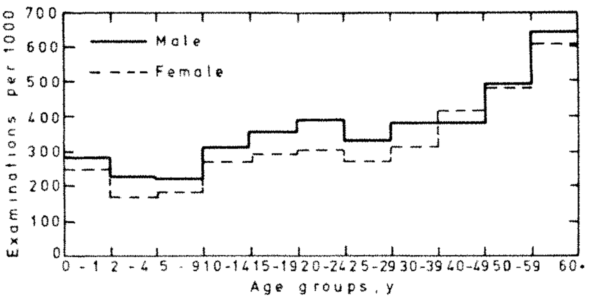


FIG. 2.

Estimated frequency per 1000 population of all types of X-ray examination (except dental) in 1977 by age and sex.

Increases in the frequency of cystography and to a lesser extent barium enemas have been balanced by a dramatic fall in the frequency of fluoroscopic examinations of the chest. Image intensifiers were reported to be used in 95% of these examinations whereas they were practically non-existent at the time of the Adrian survey. The average fluoroscopic screening times for different examinations were essentially similar to those reported by the Adrian Committee.

The variation of the frequency of diagnostic radiology with the age of the patient is shown in Fig. 2. It can be seen that the levels are highest for old people. In fact the frequency of radiological examinations per thousand for patients in their 20s has not changed much since 1957. The greatest increases have taken place in examinations of children and old people. As might be expected, individual types of examination have very different age variations. For example, examinations of the chest are commonest in older people, while those of the arm are commonest in children and young adults, and those of the skull occur at about the same frequency for all age groups.

2. *The gonadal doses*

The mean gonadal doses measured for the nine examinations which were found to be the main contributors to the GSD are shown in Table II for both sexes and for four age groups. These groupings demonstrate the general trend for considerably lower gonadal doses to be delivered to children compared with adults. There is a less clear distinction between the doses received by young adults (16–45 years) who would still have considerable child-bearing potential and those received by the over-45s for whom the likelihood of conception has reached or is rapidly approaching zero.

Not surprisingly radiography of the upper femur, hip and pelvis produced the highest mean gonadal doses for male patients, whilst fluoroscopic examinations of the lower abdomen were most important for female patients where frequently neither field size limitations nor gonadal shielding could be used to protect the ovaries.

The relationship between the mean gonadal doses measured during this survey and those obtained by the Adrian survey was found to be dependent on the age of the patient as well as the type of examination. Table III shows the ratio of current to 1957 gonad doses for all adult patients (> 16 years), where for half the types of examination no significant difference could be seen between the doses delivered now and then, while for the other half there were increases in some and decreases in others. A ratio of 1.0 indicates that the difference between the mean values for 1957 and for 1977 was less than their combined uncertainties. There was an increase of about a factor of three in the gonad dose for barium enemas since the Adrian

TABLE III

RATIO OF CURRENT TO 1957 GONADAL DOSES FOR ADULT PATIENTS

Examination	Ratio $\frac{\text{Current gonad doses}}{\text{1957 gonad doses}}$ Male	Female
Upper femur, hip	1.0	1.0
Pelvis, lumbar spine	1.0	1.0
Abdomen	1.6	0.4
Obstetric abdomen	—	0.76
IVP	0.54	0.56
Cystography	1.0	1.0
Barium meal	1.0	1.0
Barium enema	2.6	3.4

TABLE IV

RATIO OF CURRENT TO 1957 GONADAL DOSES FOR CHILDREN UNDER 16

Examination	Ratio $\frac{\text{Current gonad doses}}{\text{1957 gonad doses}}$ Male	Female
Upper femur, hip	0.59	0.27
Pelvis, lumbar spine	0.52	1.0
Abdomen	0.50	1.0
IVP	0.18	1.0
Cystography	0.30	9.5*
Barium meal	0.20	0.15
Barium enema	0.38	0.52

*Only two patients in 1957 survey.

survey, which is thought to be predominantly due to the relatively recent introduction of double-contrast techniques in fluoroscopic examinations of the colon. Indeed the number of films used in these examinations has doubled, but fluoroscopic screening times do not appear to have changed significantly, so the hoped-for reduction in dose to patients following the introduction of image intensifiers does not appear to have materialized. Obstetric abdominal examinations and intravenous pyelograms showed a definite reduction in dose, the former being the only type of examination where the use of rare-earth screens has become relatively common. Considering all the types of examination shown in Table III there would not appear to have been a substantial overall change in the level of adult gonadal exposure for the past 20 years. However, the situation for children is different as can be seen from Table IV. In this case most of the ratios are considerably less than unity and the only exception, female cystograms, is extremely dubious since the mean dose quoted in the Adrian survey is based on only two measurements and is 20 times lower than either their value for male cystograms in children or cystograms in adults of either sex. If this result is ignored it would appear that examinations on children are carried out nowadays with generally much lower gonadal doses than 20 years ago.

Clearly current practice is delivering far lower gonadal doses to children than to adults, even when only adults below the age of 45 are taken into account. Considering all the types of examination measured during the survey, the average gonadal dose per examination delivered to children was 40% of that received by adults between the ages of 16 and 45.

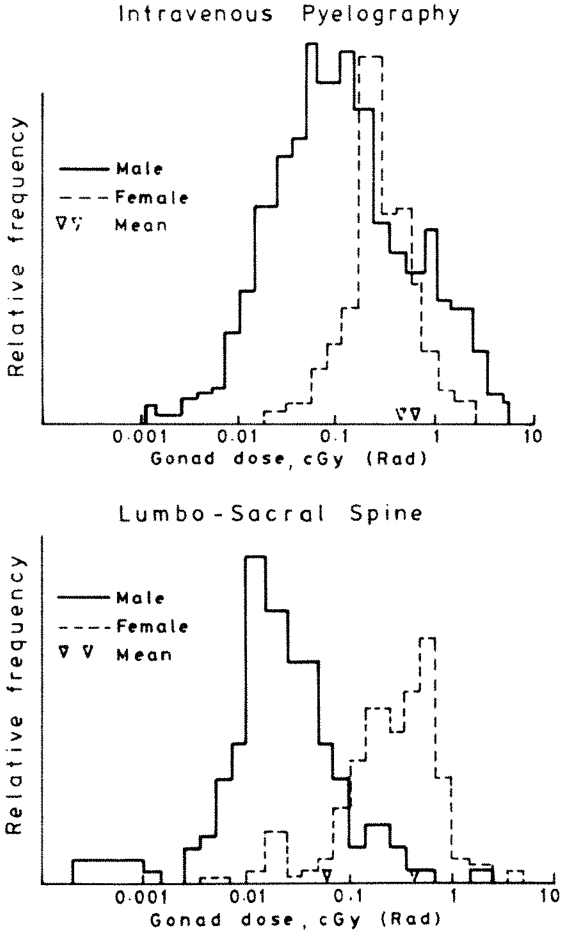


FIG. 3.

Distribution of the measured gonadal doses for intravenous pyelography and radiography of the lumbo-sacral spine.

Another interesting finding was that the enormous variability in gonadal doses for the same type of examination, which was observed to occur throughout the country during the Adrian survey, was found to persist today. Figure 3 shows histograms representing the distribution of gonadal doses measured for intravenous pyelography and radiography of the lumbo-sacral spine in the current survey. The histograms are plotted on log scales and the gonadal doses span two to three orders of magnitude for female patients and nearly four orders of magnitude for males. There were similar distributions for other types of examination with coefficients of variation ranging from 100 to 300%, and closely matching those found for the same examinations in 1957. Analysis of the within-hospital and between-hospital variances demonstrated that very large variations exist in the gonadal doses measured at individual hospitals, frequently as wide as the variations seen in the country as a whole. The mean gonadal dose delivered by different hospitals for the same category of examination and sex was significantly different for only a few of the types of examination. In these cases the difference in the mean doses amounted at most to about a factor of three.

3. *The use of gonad shields*

Information was requested on the use of gonad shields during both the examinations that were recorded for the frequency survey and those measured in the dose survey. Unfortunately, no detailed explanation was given of what was meant by a "gonad shield" and this may have led to some confusion. It was intended to include any radio-opaque device that was attached to, laid on or supported between the patient and the X-ray tube so as to shield specifically the ovaries or the testes from direct, scattered or leakage radiation. The use of adjustable beam limiting diaphragms was not meant to be interpreted as a "gonad shield" in this context. It seems unlikely however that such an interpretation was made on sufficient occasions to prejudice the data seriously.

The reported use of gonad shields was found to be extremely variable. There was considerable variation between different hospitals, between different types of examination and between different age groups. Figure 4 shows that 40% of the hospitals in the frequency survey reported the use of gonad shields in less than 10% of all examinations while two hospitals reported over 90% use. Generally it was the paediatric hospitals that indicated the greater use of shields. Variation in the use of shields between different types of examination is only to be expected. For many investigations a shield would be impractical either because it obscures vital information or because the patient has to adopt positions where its application would prove too difficult or inconvenient. For others the likely gonad dose is so low that further reduction is unnecessary or is unobtainable with the simple devices available. However, an attempt was made to see if any correlation could be found between the frequency of use of gonad shields for different types of examination and the practicability and desirability of doing so, based on the advice received from a number of experienced radiologists. No clear correlation could be found, and for examinations where it was judged to be both desirable and practicable only 20% of all patients were protected. On the other hand, a marked variation was observed depending on the age of the patient, as can be seen in Fig. 5. Gonad shields were used in about one-third of all examinations of children. A progressive decrease

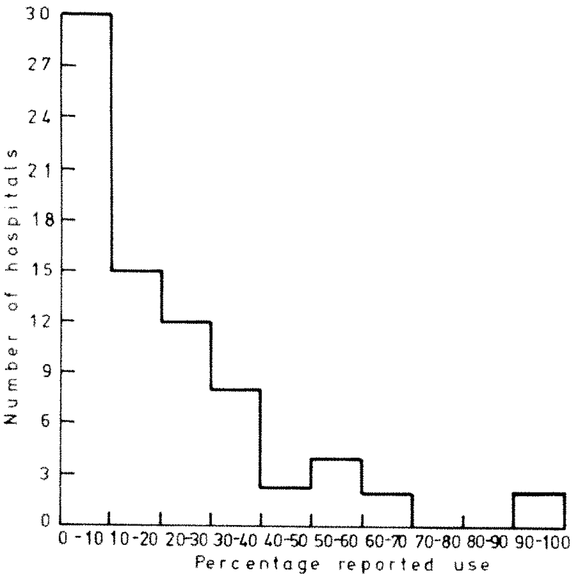


FIG. 4.

Frequency of reported use of gonad shields in different hospitals for all types of examination.

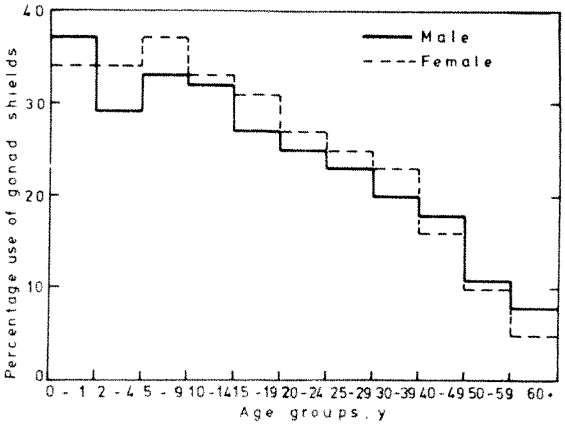


FIG. 5.

Reported percentage use of gonad shields in all examinations in 1977 by age and sex.

in the use of protective devices was seen after the age of 16 so that for patients in their 30s who still retained considerable potential for bearing children, the figure had fallen to one-fifth of all examinations. Not surprisingly, use of gonad shields dropped rapidly after the age of 50.

The reduction in gonadal dose achieved by the use of shields depends very much on the proximity of the gonads to the direct beam and on the type of shield used. Only flat radio-opaque sheets either in contact with the patient or casting a shadow over the gonads were used by hospitals taking part in the dose measurement survey. Such shields provide little protection from scattered radiation and are therefore less effective than devices that enclose the testes, particularly when they lie outside the direct beam. However, the gonadal doses for examinations of the abdomen, lumbar spine, pelvis and intravenous pyelograms were on average reduced by 75% for men and by 70% for women when gonad shields were used for all or part of the examination. This is a substantial reduction, and a large impact could be made on the GSD if the use of shields during these types of examination was increased, because of their large contribution to the population genetic dose.

Gonad shields do not of course provide the only, or even the best, means for reducing genetic doses. Precise beam collimation, the use of imaging systems with the optimum sensitivity, and the avoidance of unnecessary exposures, can all be extremely effective in providing protection to the patient and in many situations will be more important than the use of shields. However, the effectiveness of these other techniques could not be ascertained from the data collected for this survey as this assessment was not one of the survey's specific objectives. In view of the very wide range of gonadal doses observed it may be considered necessary to initiate further work with the objective of identifying whether the large range can be related to specific factors of technique or whether it is mostly due to differences in physique and pathology of the patients. No correlation could be found between gonad doses and the limited data on physique collected during the gonadal dose survey. There is evidence from other surveys of diagnostic X-ray techniques, both in this country and abroad, that if differences between patients are eliminated by substituting a standard phantom, there remains considerable variation in the doses delivered by different practitioners. The Nationwide Evaluation of X-ray Trends (NEXT) programme has been in operation in the USA since 1972. In this programme operators of diagnostic X-ray equipment are asked to select their usual techniques for conducting a particular examination on a well-defined "standard-sized" adult patient and then exposure measurements are made and organ doses calculated for this standard patient. The wide range of technique factors that were found to be employed for a relatively simple examination like an AP lumbosacral spine led to ovarian doses ranging over a factor of 200 and testicular doses ranging over a factor of 3000 (Gaskill *et al.*, 1974). Consequently, heterogeneity of patients would not appear to be the major cause for variability in gonadal dose.

4. *The Genetically Significant Dose*

The annual GSD from diagnostic radiology in National Health Service (NHS) Hospitals in 1977 is estimated to be 113 μGy (11.3 mrad) with a standard error of about 12 μGy (1.2 mrad). Additional contributions to the GSD from radiology conducted other than in NHS hospitals are given in Table V. These bring the estimated total GSD from diagnostic radiology in 1977 up to 120 μGy (12 mrad).

The corresponding total for the 1957 national survey was 141 μGy (14.1 mrad). Although this is slightly higher than the present estimate, the difference is less than twice its standard error, and there are also methodological differences between the two estimates which may have led to a lower value for 1977. One principal difference between the two surveys arises from the separation of the gonadal doses into three age groups for the important examination types in the 1977 survey, whereas data on only two age groups (children and adults) were available in 1957. By distinguishing between adults of child-bearing age and older people, who generally receive higher gonadal doses (Table II), a lower and more realistic estimate of the GSD has been made than otherwise would have been the case. If all adults had been considered together in a single age group the GSD would have been about 15% higher (~140 μGy), bringing it very close to the 1957 estimate. Therefore there is no evidence of a change in the

TABLE V

The contributions to the GSD from diagnostic radiology practised within and outside the NHS

Source	GSD (μGy/yr)
NHS hospitals	113
Armed forces	2.2
Private hospitals	1.7
Private practice	1.3
Dental radiology	0.3
Total	~120

TABLE VI

Estimated contributions to the GSD from the more important types of examination in NHS hospitals for males females and fetuses. A comparison of the 1957 and 1977 national surveys

Examination	Contribution to GSD (μGy/yr)							
	1957				1977			
	Male	Female	Fetal	Total	Male	Female	Fetal	Total
Pelvis and lumbo-sacral area	17	12	2	31	13	15	1	30
Upper femur and hip	13	1	0	15	15	1	0	15
Urography	10	7	1	17	5	7	1	13
Cystography	0	0	0	1	6	5	0	12
Barium enema	0	1	0	2	1	8	1	9
Abdomen	2	3	1	6	6	4	0	9
Obstetric abdomen	0	17	29	45	0	2	4	6
Other	6	9	1	15	9	7	2	19
Total	48	50	34	132	55	49	9	113

level of the annual GSD from diagnostic radiology over the last 20 years.

The contributions to the GSD from the various types of examination carried out in NHS hospitals are shown in Table VI for males, females and fetuses, both for the previous survey and the current one. The present pattern is broadly similar to that occurring 20 years ago except that there has been a dramatic fall in the contribution from examinations of the obstetric abdomen and large increases in the contributions from cystography and barium enemas. The fall in the contribution from obstetric examinations is due to reductions in both the frequency of these examinations and in the gonadal doses delivered per examination. The increased contribution from cystography is due chiefly to an increase in its frequency, while the increased contribution from barium enemas is a reflection of the increased number of complex investigations of the colon which result in higher ovarian doses per examination. Despite these changes, the contributions to the total GSD from male and female patients remain remarkably similar over the 20-year period, while the contribution from fetuses has fallen by a factor of almost four. This drop is due almost entirely to the decrease in importance of obstetric examinations.

Examinations of children are responsible for about one-quarter of the GSD. This is rather less than would be expected from a consideration of the relative number of children and adults in the population (the number of children under 15 is 55% of the number of adults between 16 and 45), despite the fact that the former have a higher child expectancy. Differences in frequency of examinations account for only a part of this effect, the main reason being the substantially lower gonadal doses that children receive per examination. The *per caput* gonadal dose for children is only one-fifth of that for adults of child-bearing age.

Separate estimates of the GSD were made for England, Scotland and Wales but no significant differences were found between the values for each country.

Discussion

At first sight it might seem surprising that over the last 20 years the GSD has remained stable although the frequency of radiological examinations per head of the population has increased by about 50%. Three factors account for this. Firstly, although a consistent trend towards lower doses per examination is not evident when adult patients are considered, there is a marked reduction in the doses given to children for nearly all types of examination. Secondly, obstetric radiology, which was the most important single contributor to the annual GSD in 1957, providing 45 out of the total of 141 μGy, now contributes only 6 μGy. Thirdly, although the overall increase in frequency of examinations of all types has been about 50%, much of this increase has occurred in patients who are beyond child-bearing age. Such examinations do not contribute to the GSD.

It might seem fair to conclude that, since this level of population gonadal exposure from diagnostic radiology was considered acceptable by the Adrian Committee in 1960, the situation probably remains satisfactory today. This presupposes however that our appreciation of the genetic risks associated with ionizing radiation has remained unchanged over 20 years. The recommendation of the Adrian Committee that there was no need for any major restrictions in radiological practice was based on two conclusions of a report published by the Medical Research Council in 1956. These were, firstly, that the maximum amount of additional radiation which may be received by the population as a whole, without giving rise to concern, is unlikely to be more than twice the natural background dose, *i.e.* 6 rad per generation; secondly, doses up to, and somewhat beyond, the "doubling dose" for genetic effects (then assessed to be about 50 rad) from conception to the age of 30 years, need give no concern to the individual as regards his own offspring. Since the GSD from all branches of medical radiology was about 20 mrad per year, leading to only 0.6 rad per generation averaged over the whole population, and since the dose to the gonads for any X-ray examination was very small in comparison with the 50 rad "doubling dose", there indeed did not appear to be any serious cause for concern.

Current estimates of the probability of serious genetic defects following exposure to ionizing radiation assume a "doubling dose" of 1 Gy (100 rad) (Oftedal and Searle, 1980), based on experimental work with mice. Analysis of the naturally-occurring frequencies of the various types of serious genetic defects in human populations in combination with this "doubling dose" have been used to estimate an overall risk factor for the transmission of serious hereditary ill health to future generations. This has been published in ICRP Report 26 where a value of $10^{-2}\mathrm{Sv}^{-1}$ is quoted for the probability of serious defects appearing in the first two generations with an additional equal probability for all succeeding generations.

Although the promulgation of such universally applicable risk factors allows the calculation of the likely extent of the genetic consequences from any source of gonadal exposure, such estimates must be treated with considerable reservation. Many large uncertainties surround the data used in the derivation of these factors and many assumptions have to be made to arrive at a single figure for use in all circumstances. Not the least assumption is that results obtained with laboratory animals are applicable to man. Nonetheless, such an imprecise estimate may serve the useful purpose of placing the genetic risks of diagnostic radiology into some form of perspective, even if it is realized that it may well be in error by an order of magnitude either way.

Taking the annual value of the GSD to be 120 μSv and the risk factor for genetic injury in all future generations to be 2.10^{-2} per sievert received by either parent, then from equations (1) and (2)

$$\text{total annual genetic injury to population} = \alpha \text{GSD} \times \Sigma P_i$$

ΣP_i is twice the number of children expected from the present population. Referring to the child-expectancy figures of Taylor and Webb (1980)

$$\Sigma P_i = 42.10^6$$

$$\therefore \text{total annual genetic injury to population} = 2.10^{-2} \times 120.10^{-6} \times 42.10^6 = 100 \text{ cases.}$$

In view of the generally conservative assumptions made in the derivation of this number, it seems more likely that it will represent an over-estimate of the true consequences of diagnostic radiology rather than an underestimate. For comparison, UNSCEAR (1977) estimates that about 10% of all live births will experience some form of genetic disorder in the course of their lives. In Great Britain this amounts to about 60000 births annually, but not all of these disorders will be as serious as those predicted by the hereditary risk factor recommended in ICRP 26.

Comparison with other countries and with other sources of population exposure may further serve to place the contribution of diagnostic radiology in Great Britain into a sharper perspective. Figures obtained during the past ten years for the frequency of X-ray examinations and the GSD in overseas countries are shown in Table VII. Rigorous comparisons would be unjustified in view of the differences in the methods used to derive the figures for each country and the large associated uncertainties, some of which are mentioned in the last column of the Table. Notwithstanding this proviso it is still apparent that the GSD for Great Britain is considerably lower than those published for other developed nations. One obvious cause for this is the relatively low annual frequency of diagnostic examinations per thousand head of population in Britain. Closer scrutiny of the data reveals that the gonad doses in the UK are in general at least as low as in other countries with sophisticated radiological services except possibly in Japan. Although the frequency of examinations in Japan is towards the high end of the range, it is notable that the GSD has been maintained at the relatively low level of 170 μGy (17 mrad). It is perhaps not merely coincidental that the literature contains a disproportionately large number of papers from Japan dealing with radiological protection in medicine. In contrast, the figures for the GSD from some of the developing countries are rather higher than would be expected on the basis of the reported frequency of diagnostic examinations.

The relative contribution of diagnostic radiology to the total GSD received by the population of Great Britain from all major sources of gonadal exposure is shown schematically in Fig. 6. Values for the other contributors are taken from the report of

TABLE VII

ESTIMATED CONTRIBUTION TO THE GSD FROM DIAGNOSTIC RADIOLOGY IN A NUMBER OF COUNTRIES WITH THEIR POPULATION AND ESTIMATED ANNUAL FREQUENCY OF EXAMINATION PER THOUSAND POPULATION

Country	Year	Population × 10⁶	Annual no. of exams per 1000 population					Annual GSD (μGy)	Reference	Comments
			Radi-ography	Fluor-oscopy	Mass survey	Dental	Total excluding dental ( ) = incomplete			
India	1967–72	550	35				(35)	11	Supe *et al.*, 1974	Thorough. Freq. sample 120000 patients. Dose sample 15000 patients
Italy	1974	55	363		75	72	438	~300	Benassai *et al.*, 1977	Freq. sample 10%, most doses from literature. GSD only approx., possible error ±300
Romania	1970	20.5	238	322	452		1012	290	Racoveanu *et al.*, 1973	Freq. sample 492000 exams. Dose sample 24000 patients
Puerto Rico	1968	3	502	40	56		598	430	Gileadi, 1975	Higher gonadal doses than Britain account for higher GSD
Switzerland	1971	6.3	1350				(1350)	430	Poretti *et al.*, 1971	Freq. sample 60000 patients, doses measured at various hospitals
Sweden	1974–76	8.1	540		110	1500	650	460	Bengtsson *et al.*, 1978	High gonadal doses for important exams. probably account for high GSD
Netherlands	1972	12.6	890		250		1140	280	Koen and Weber, 1973	Freq. data for 1967 × 1.10. Doses measured for male patients only. Accuracy of GSD doubtful
Japan	1974	108	676	134			(810)	170	Hashizume *et al.*, 1976	Lower gonadal doses than GB, hence low GSD for high frequency
USA	1970	195	646					200	US DHEW, 1976	No data on fluoroscopic exams. or mass min. GSD for radiography only
West Germany (Hamburg)	1974	1.8	1530		128		1658	410	UNSCEAR, 1977	Figures as reported in UNSCEAR 1977
Iraq	1972	10	158		42	15	200	520	Abbas, 1973	Freq. sample 1000 patients, doses calculated for only 70 patients. Accuracy of GSD doubtful
Great Britain	1977	55	390	25	25	110	440	120	Present work	

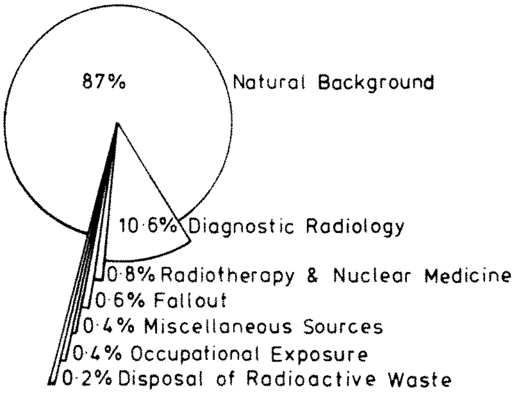


FIG. 6.

The relative contributions of different sources to the total GSD received by the population of Great Britain in 1977.

Taylor and Webb (1978). The GSD from all forms of diagnostic radiology amounts to 12% of that from natural background radiation, which is comparable in magnitude to the difference in levels of background radiation received by people living in different parts of Great Britain. On the other hand, it is responsible for 87% of all man-made sources of the population's genetic exposure.

CONCLUSIONS

It would seem reasonable to conclude that the current situation in Great Britain is broadly satisfactory for, notwithstanding a substantial increase in the frequency of X-ray examinations, the probability of serious hereditary defects being passed on to future generations has not significantly changed in 20 years and would appear to be considerably lower than that found in comparable industrialized countries.

A level of no more than 100 cases of serious genetic injury per year, in comparison with the 60000 cases of genetic disorder that occur naturally, would appear to be justified in terms of the undoubted benefits conferred upon society by the practice of diagnostic radiology. Any major restrictions imposed upon these services are likely to result in more suffering than they could reasonably hope to prevent.

However, there is some evidence from the data collected for this reappraisal that radiological protection practices could be improved so as to reduce the genetic consequences still further with no detriment to the care of patients. The very large variability found in individual gonadal doses for the same type of examination, together with the observation that examinations could be satisfactorily conducted on children with a much higher degree of gonadal protection than that given to young adults, both suggest that some patients could be receiving doses that are unnecessarily high.

A 15% reduction in the contribution from diagnostic radiology would have the same effect on the total GSD to the population of Britain as eliminating all other man-made sources of ionizing radiation completely. Considering the large investment in radiological protection in other fields such as the nuclear-power industry, the relatively modest expenditure required to achieve a small but very significant reduction in medical exposures would seem to be justified. It is a fundamental precept in radiological protection that all exposures, however small, should be reduced until economic or social factors intervene to make further reduction unprofitable (ICRP, 1977).

The surveys carried out for this reappraisal of the GSD were not designed specifically to identify those practices or techniques leading to high gonadal doses. However, it became apparent that the pattern of use of gonad shields was somewhat erratic, and their more consistent employment on patients of potential child-bearing age would be one simple method of effecting an appreciable reduction in gonadal exposure. The more widespread use of rare-earth screens and improvements in some hospitals in the facilities for providing precise beam collimation would also considerably reduce the amount of radiation received by patients.

There would seem to be a need for further investigations to identify the parameters of technique responsible for the large variation in gonadal doses. Also a simple method for routinely assessing the relative risk of X-ray examinations, so that individual practitioners could readily compare their own performance with the national pattern, might well increase the opportunities for identifying and reducing sources of high exposures of patients. Such developments are being given active consideration in the NRPB's continuing medical dosimetry programme.

ACKNOWLEDGMENTS

This survey would not have been possible without the willing co-operation of people too numerous to detail here. We are particularly grateful to the radiologists, radiographers and physicists at the participating hospitals who, in addition to their normal heavy duties, undertook the extra work of providing us with data.

A special working group was convened to advise the authors on all aspects of the survey from the planning stages onwards and we would like to express our gratitude to them. Professor R. E. Steiner was Chairman of the group and its members included Dr. G. M. Ardran, Professor R. E. Ellis, the late Professor R. Oliver, Dr. R. Oliver, Dr. S. Osborn and Dr. K. A. Rowley.

We would like to acknowledge the help of the Directors-General of the Medical Services of the Armed Forces, the staff of mass-miniature radiography units and hospitals outside the National Health Service and the chief medical officers of a number of industries for providing us with much information.

Our thanks are due to the Office of Population Censuses and Surveys for allowing us access to information concerning the national population in advance of its general release. Special mention must be made of the contribution of the Department of Health and Social Security statisticians, Mr. M. Sharratt who selected the sample for the frequency survey, and Ms. W. McLean.

Finally, we are especially grateful to Mrs. E. S. Fisher, Mr. S. V. Harries, Dr. P. C. Shrimpton and other colleagues at the NRPB who devoted so much time to the onerous tasks of providing the necessary dosemeters and performing the data analysis.

REFERENCES

ABBAS, M. S., 1973. Use of medical X-ray diagnostic units in Iraq. In *Proceedings 3rd International Congress, IRPA, Washington DC, 1973.* USAEC, CONF-730907.

ADRIAN, LORD, 1960. Radiological hazards to patients; Second Report of the Committee under Lord Adrian (HMSO, London).

BENASSAI, S., DOBICI, F., SUSANNA, A., INDOVINA, P. L., PUGLIANI, L. and SALVADORI, P., 1977. Some results on radiation exposure of the Italian population due to medical diagnostic examination in 1974. *Health Physics, 32*, 403.

BENGTSSON, G., BLOMGREN, P. G., BERGMAN, K. and ABERG, L., 1978. Patient exposures and radiation risks in Swedish diagnostic radiology. *Acta Radiologica Oncology, 17*, 81.

COUNCIL OF THE EUROPEAN COMMUNITIES, 1976. The revised basic safety standards for the health protection of the general public and workers against the dangers of ionising radiation; Council Directive of 1 June 1976. *Official Journal of the European Communities*, No. 1187, 12 July 1976.

DARBY, S. C., KENDALL, G. M., RAE, S. and WALL, B. F., 1980. The genetically significant dose from diagnostic radiology in Great Britain in 1977. National Radiological Protection Board, Harwell, Report No. NRPB R-106 (HMSO, London).

GASKILL, J. W., PAKENAS, W. P. and BLACKBURN, J. A., 1974. Nationwide Evaluation of X-ray Trends (NEXT): an organ dose index system for evaluating the effectiveness of X-ray control programs. In *Proceedings of the 13th International Congress of Radiology*, Madrid, 1973 (Excerpta Medica, Amsterdam).

GILEADI, M., 1975. Summary: Islandwide radiation survey in Puerto Rico, 1968–1973 (Puerto Rico Nuclear Centre, Mayaguez, Puerto Rico).

HASHIZUME, T., MARUYAMA, T. and KUMAMOTO, Y., 1976. Estimation of population doses from diagnostic medical examinations in Japan, 1974. 2. Estimation of genetically significant dose. *Nippon Acta Radiologica, 36*, 208.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION, 1977. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. *Annals of the ICRP, 1*, No. 3 (Pergamon Press, Oxford).

KENDALL, G. M., DARBY, S. C., HARRIES, S. V. and RAE, S., 1980. A frequency survey of radiological examinations carried out in National Health Service hospitals in Great Britain in 1977 for diagnostic purposes. National Radiological Protection Board, Harwell, Report No. NRPB R-104 (HMSO, London).

KENDALL, G. M., DARBY, S. C. and RAE, S., 1981. The level of dental radiography in Great Britain. *British Dental Journal* (in press).

KOEN, J. A. and WEBER, J., 1973. The genetically significant dose due to medical X-ray examinations in the Netherlands. In *Proceedings of the 3rd International Congress of the IRPA, Washington DC*, 1973. USAEC, CONF-730907.

MEDICAL RESEARCH COUNCIL, 1956. The hazards to man of nuclear and allied radiations. Cmnd. 9780 (HMSO, London).

OFTEDAL, P. and SEARLE, A. G., 1980. An overall genetic risk assessment for radiological protection purposes. *Journal of Medical Genetics, 17*, 15–20.

PORETTI, G. G., IONESCO-FARCA, F. and LANZ, W., 1971. Die Strahlenbelastung der Schweizer Bevoelkerung infolge roentgendiagnosticher Untersuchungen. (Universitätsabteiling für medizinische Strahlenphysik, Inselspittal, Bern, Switzerland).

RACOVEANU, N. T., DIACONESCU, C., MODORAN, G., VASILESCU-FULEA, C., PLAVOSIN, P. and MILU, C. G., 1973. Medical irradiation of the population in Romania during 1970. In *Proceedings of the 3rd International Congress of the IRPA, Washington DC, 1973.* USAEC, CONF-730907.

SUPE, S. J., RAO, S. M., SAWANT, S. G., JANAKIRAMAN, G. and GANESH, A., 1974. Genetically significant dose to the population in India from X-ray diagnostic procedures. In *Proceedings of the Seminar on Population Dose Evaluations and Standards for Man and His Environment, Portoroz, May 1974* (International Atomic Energy Agency, Vienna).

TAYLOR, F. E., 1980. Estimation of child expectancy for the population of the United Kingdom in 1974 to be used in the calculation of genetically significant dose. National Radiological Protection Board, Harwell, Report No. NRPB-M49 (HMSO, London).

TAYLOR, F. E. and WEBB, G. A. M., 1978. Radiation exposure of the UK population, NRPB, Harwell, Report No. R77 (HMSO, London).

UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION (UNSCEAR), 1972. *Ionizing Radiation: Levels and Effects. Volume 1: Levels* (United Nations, New York).

UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION (UNSCEAR), 1977. *Sources and Effects of Ionizing Radiations* (United Nations, New York).

US DEPARTMENT OF HEALTH, EDUCATION AND WELFARE, 1976. Gonad doses and genetically significant dose from diagnostic radiology, US, 1964 and 1970. DHEW (FDA), Rockville, Md, 76-8034.

WALL, B. F., FISHER, E. S., SHRIMPTON, P. C. and RAE, S., 1980. Current levels of gonadal irradiation from a selection of routine diagnostic X-ray examinations in Great Britain. National Radiological Protection Board, Harwell, Report No. NRPB-R105 (HMSO, London).

1981, *British Journal of Radiology*, *54*, 731–735 SEPTEMBER 1981

Coronary collateral response and myocardial function

By J. K. Walker, M. D., F.R.C.R.

Cardiovascular Unit, Groby Road Hospital, Groby Road, Leicester LE3 9QE

P. R. M. Jones, M. Sc., Ph.D., D.C.R., M.I.Biol. and R. H. Harding, M.Sc., C.Eng., M.I.E.R.E.

Human Biology Laboratory, Department of Human Sciences, University of Loughborough, Leicestershire LE11 3TU

(*Received January 1981*)

ABSTRACT

Two hundred and twelve patients with recognizable coronary artery block and no other pathology were selected using an interactive computer data retrieval system. The relationship of coronary artery collaterals to left ventricular (LV) dysfunction was investigated. Analysis revealed the significant role of the left anterior descending (LAD) coronary artery and collateral development to the preservation of LV function.

This study underlines the value of radiological observation when subject to statistical scrutiny.

The role of coronary collaterals as contributors to left ventricular myocardial perfusion has been debated during the past decade but with no conclusion. Some studies (Baltaxe and Gensini, 1973; Bemis *et al.*, 1973; Bing and Hellberg, 1972; Bodenheimer *et al.*, 1977; Helfant *et al.*, 1970, 1971; Knoebel *et al.*, 1972) deny that they make any contribution at all, whilst others claim evidence to prove that the coronary collateral circulation provides a significant compensatory mechanism (Aloan *et al.*, 1977; Cohen, 1978; Flameng *et al.*, 1978; Frick *et al.*, 1976; Hecht *et al.*, 1975; Helfant *et al.*, 1977; Levin *et al.*, 1973; Schaper *et al.*, 1973; Shakhov, 1978). McGregor (1975) believed that it was the unreliability of the indirect method, *i.e.* angiocardiography, which led to this disagreement and commented that to pursue it was unlikely to be profitable.

We believe that indirect observations, even when the variables are many and complex, are valid provided that they are made on a large sample. Because we have cardiac investigative data from this unit stored on computer, we felt we were in a position to undertake this study.

Our aim was to define critical coronary artery obstruction and to determine if collaterals help myocardial perfusion and preserve myocardial function.

SUBJECTS AND METHODS

A total of 606 consecutive patients having a full cardiac investigation, including catheterization and angiocardiography, was studied. Of these 307 had significant atheroma and 212 had no other known pathology. The age range was 28 to 70 years. All patients had left heart catheterization via the right femoral artery. Routine blood pressures and oxygen saturations were measured. Left ventricular cine angiography in the right anterior oblique (RAO) position was carried out using a National Institute of Health (NIH) No. 8 disposable catheter. Forty millilitres of Cardio-Conray (May & Baker) were injected. Selective coronary arteriography, using the Judkins technique, was carried out. Analysis of left ventricular wall motion was made subjectively on a 35 mm cine projector and dysfunction was graded mild, moderate, severe and gross, using values 0 to 4.

Occlusion of the three main coronary arteries, the left anterior descending (LAD), the circumflex (CIRC) and the right coronary artery (RCA) were graded conventionally, 50%, 70%, 90%, 100%, using values 0 to 4.

The extent of collateral development was more difficult to grade subjectively. Grade 0 with no collaterals, and grade 4 where all branches filled instantly via large collaterals, were easily defined. Grade 1 was defined as a myocardial blush and/or the opening of minimal epicardial collaterals, but where the distal blocked artery was never visible. Grade 2 was where the distal blocked artery was partially visible, grade 3 where the distal blocked artery was fully visible or where it was supplied by myocardial bridge collaterals.

Age, duration of symptoms, and mortality were also recorded. The characteristic difficulty, which becomes apparent from a survey of the literature, is the simultaneous comparison of three variables: left ventricular function, collateral response, and coronary occlusion, of which the latter is a compound of three arteries of differing importance and variable obstruction (Fig. 1). The literature generally agrees that the LAD supplies twice the myocardial mass of the CIRC or the RCA (Brandt *et al.*, 1977), so a system of scoring was evolved by which the four grades, 1, 2, 3 and 4 were added together with the LAD score doubled, giving a possible score of 16.

For the analyses of results, the data were subjected to factorial analyses using both varimax and oblique structure matrices, in order to determine which indices should be used in step-down multiple regression analysis. The 5% level of significance was accepted as significant.

RESULTS

Table I shows the mean values and standard deviations of all variables studied. Figure 2 shows the coronary collateral artery occlusion score regressed on left ventricular dysfunction. Whilst the correlation coefficient is significant ($p < 0.001$), the magnitude is low ($r = 0.27$), indicating that approximately 92% of the variance is unaccounted for. Further it shows that at grade 1, where function of the left ventricle (LV) begins to fail, a score of 9.5, equivalent to more than 90% occlusion of the LAD artery, is critical.

Figure 3 compares the coronary artery occlusion score with collateral artery response; it shows a significant correlation $r = 0.60$, $p < 0.001$. When coronary collateral development is compared with left ventricular dysfunction (Fig. 4), a low non-significant negative correlation ($r = -0.04$) results.

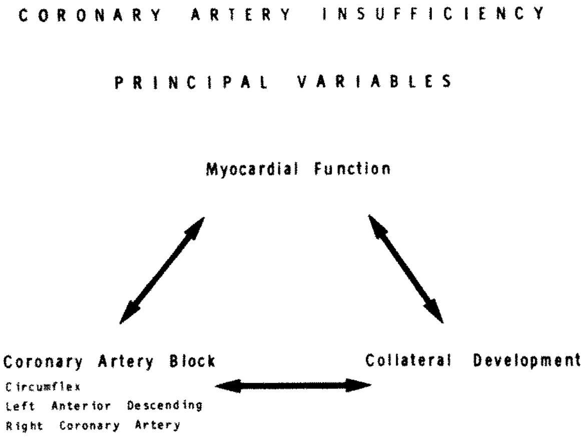


FIG. 1.

A flow diagram illustrating the interaction of complex variables.

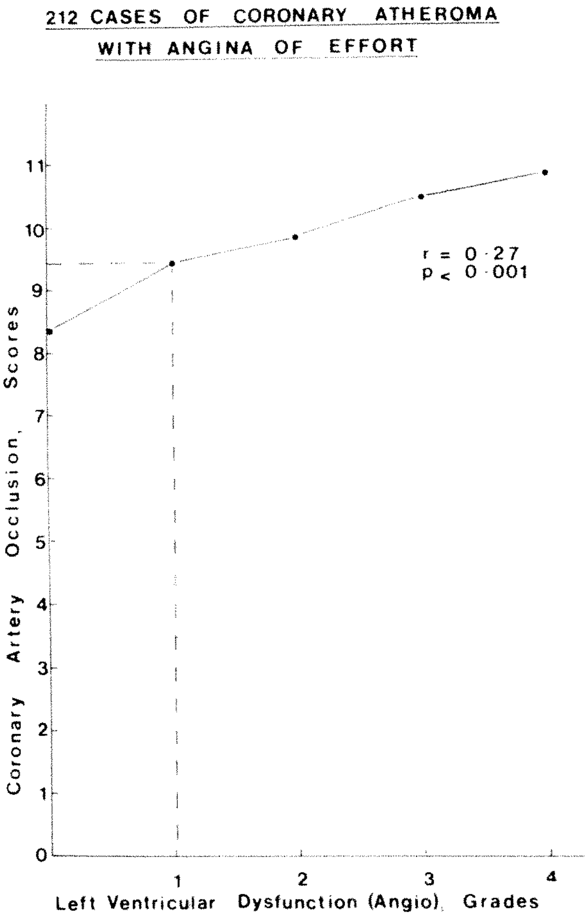


FIG. 2.

The relationship of coronary artery block (CAB) to LV function. Dotted line is shown defining significant CAB.

TABLE I

DETAILS OF THE PATIENTS HAVING FULL CARDIAC INVESTIGATION, INCLUDING MEAN VALUES AND RANGES FOR THE INDICES USED IN THE ANALYSIS

Index	Unit	Mean	$n = 212$ S D	Range
Age	a	51.8	8.9	28 –70
Duration of symptoms	a	3.2	2.9	0.5– 9
Circumflex artery, occlusion grades	0 to 4	1.7	1.3	0– 4
Left anterior descending artery	0 to 4	2.7	1.2	0– 4
Right coronary artery	0 to 4	2.3	1.6	0– 4
Grades of collateral arteries development	0 to 4	2.1	1.5	0– 4
Left ventricular dysfunction, grades	0 to 4	1.4	1.4	0– 4

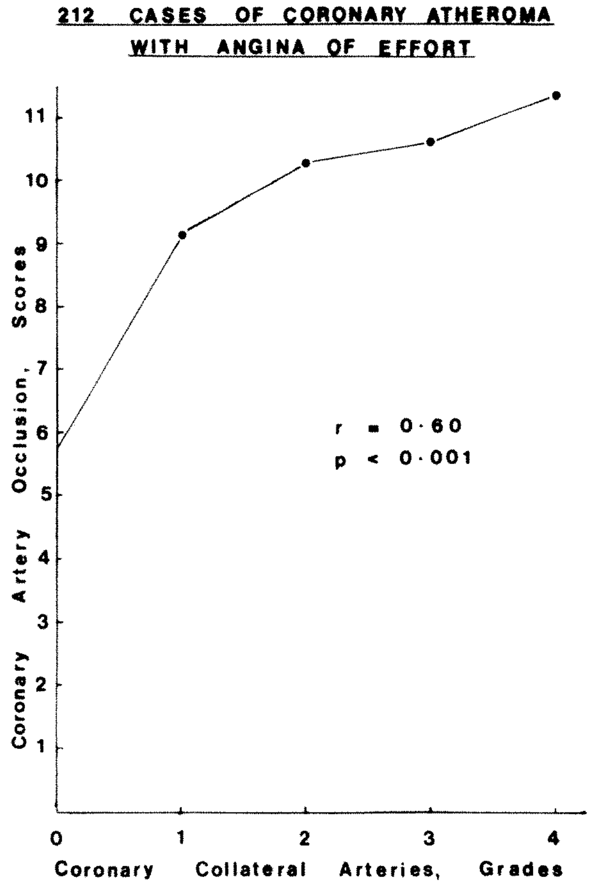


FIG. 3.

The good relationship of coronary artery collateral development (CACD) to CAB in a large series.

Table II gives the multiple regression equations for the indices of LV dysfunction on age, duration of symptoms, mortality, occlusion and collateral artery development, together with the multiple correlation

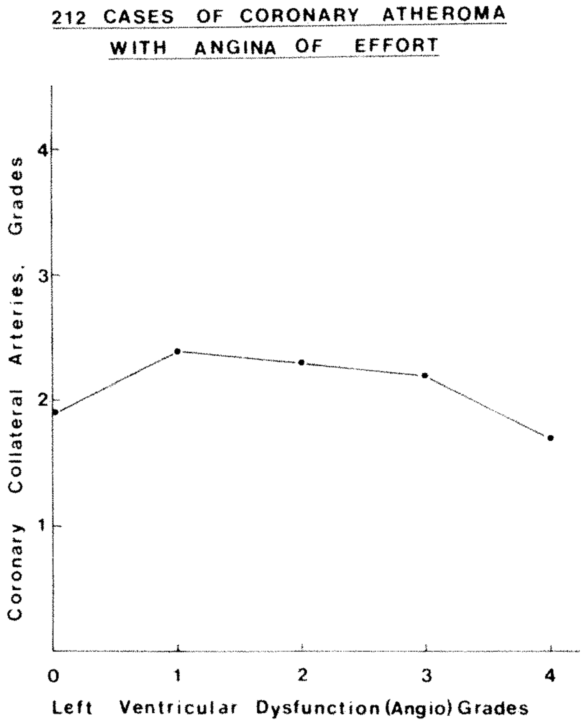


FIG. 4.

The poor correlation between CACD and LV function when considered in isolation.

TABLE II

MULTIPLE REGRESSION (R) EQUATION WHICH BEST DESCRIBES THE LV DYSFUNCTION IN TERMS OF THE 7 MEASURED VARIABLES

LV Dysfunction (Y)	+ :ON: +	Age +	Duration of symptoms +	Mortality +	Circumflex artery +	LAD +	RCA +	No. of collateral arteries
		(×1)	(×2)	(×3)	(×4)	(×5)	(×6)	(×7)
	Intercept	Regression coefficients						
	−0.871	0.024 *	−0.036 ns	0.047 ns	0.101 ns	0.331 ***	0.117 *	−0.140 *

$R = 0.363$***; SEE = ±1.35.
Levels of significance:
*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$
ns not significant.

coefficient (R) and the residual standard error of the estimate (SEE) for the equation. Here also the relative importance of two main coronary arteries is indicated by their significant terms, but with the LAD artery showing considerable dominance over the RCA by virtue of its greater level of significances ($p < 0.001$). Also illustrated are two further significant terms: age and the number of collateral arteries. It can be seen that there are three non-significant terms in the equation: duration of symptoms, CIRC and mortality. In order of magnitude of the computed t value they have been removed from the analysis by step-down multiple regression (Fig. 5, Table III).

DISCUSSION

The "problem" of the role of coronary artery collaterals is the problem inherent in a situation where many variables are operating simultaneously. Earlier authors using various criteria concluded that coronary artery collaterals made little contribution to myocardial perfusion and myocardial function. In these circumstances it is perhaps understandable that a reviewer should conclude that the indirect method was unlikely to give the answer (McGregor, 1975).

More recently, workers using detailed measurements (Hecht *et al.*, 1975), matched subject groups differing only in the extent of the collateral response (Aloan *et al.*, 1977; Lavine *et al.*, 1974; Shakhov, 1978), the use of isotopes (Frick *et al.*, 1976; Schaper *et al.*, 1973) and even the direct measurement of distal coronary artery pressure during surgery (Flameng *et al.*, 1978) supported the opposite view that coronary artery collaterals do make a significant, but undefined, contribution. The good correlation between coronary artery block (CAB) and coronary artery collateral development (CACD) shown in

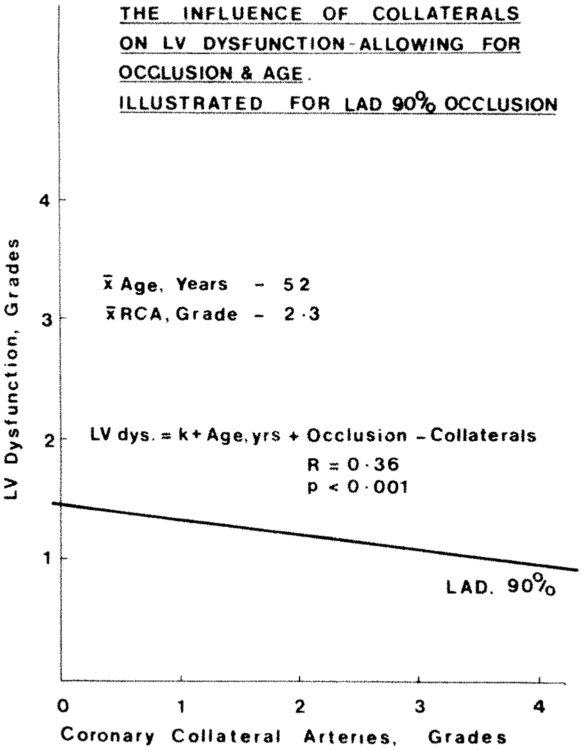


FIG. 5.

The significant multiple correlation between LV dysfunction and CACD when other significant variables are included in the equation.

TABLE III

THE MULTIPLE VARIABLES WHICH BEST DESCRIBE LEFT VENTRICULAR DYSFUNCTION IN 212 PATIENTS WITH SIGNIFICANT ATHEROMA

LV dysfunction (Y)	+ :ON:	+ Age (×1)	+ LAD (×2)	+ RCA (×3)	+ No. of collateral Arteries (×4)
	Intercept	Regression coefficients			
	−0.876 *	0.025 **	0.357 ***	0.141 *	−0.130 *

$R = 0.357$; SEE $= \pm 1.35$.
Levels of significance:
*** $p < 0.001$
** $p < 0.01$
* $p < 0.05$

Fig. 3, whilst not directly relevant, gives confidence that the subjective observations have validity.

It would seem logical, in a situation where the main problem was the large number of interacting variables, that if a large enough number of subjects were studied, by a statistical method which took account of all the relevant factors, an answer could be forthcoming. In this respect, step-wise multiple regression analysis, when applied to our data, has not only established the role of collateral arteries in myocardial perfusion—it has also defined the importance of the other significant contributory variables. It is interesting that the contribution made by one of the independent variables, the circumflex artery, is non-significant and was dropped from the regression procedure. Two of the original variables, duration of symptoms and the mortality, had computed t values close to the 5% level of accepted significance, so it should be borne in mind that with larger numbers, duration of symptoms and mortality may be shown to be important. Preliminary analysis shows that in those with symptoms of over five years, and grade 1 LV dysfunction and grade 2 or more CACD, the mortality is low—approximately 6% per annum.

Coronary collateral development relates inversely to LV dysfunction, with a small but significant multiple correlation coefficient of $R=0.357$ ($p < 0.001$), when taken with age and CAB.

We recognize that there must be other factors less clearly defined which should be taken into account to explain the variance of 87% ($1-R^2$). Such factors may be: site of occlusion in relation to other arteries, and speed of development.

In conclusion we think that one of the most useful characteristics of this interactive computer system is that it allows analysis of the type of complex data which is commonly presented in our routine work.

ACKNOWLEDGMENTS

We are grateful to Maureen Tomlinson and Nick Smith, Department of Human Sciences, University of Loughborough, for their assistance with the data preparation and computing, and would also like to thank the Department of Medical Illustration of Leicester University Medical School.

REFERENCES

ALOAN, L., TRUFFA, M., ANACHE, M., CABRAL, H., CARVALHO, M. and CARNIRO, R. D., 1978. Circulacao colateral e contratilidade ventricular en lesoes da arteria descendente anterior. *Arquivos Brasilieros de Cardiologia*, *31*, 167–171.

BALTAXE, H. A. and GENSINI, G., 1973. Coronary collateral circulation its description and importance. *C.R.C. Critical Reviews in Clinical Radiology and Nuclear Medicine*. (C.R.C. Press, West Palm Beach, Florida), pp. 219–233.

BEMIS, C. E., GORLIN, R., KEMP, H. G. and HERMAN, V. H., 1973. Progression of coronary artery disease. *Circulation*, *47*, 455–463.

BING, R. J. and HELLBERG, K., 1972. Coronary blood flow in relation to angina pectris. *Circulation*, *46*, 1146–1152.

BODENHEIMER, M. M., VIDYA, S. B., HERMANN, G. A., TROUT, R. G., PASDAR, H. and HELFANT, R. H., 1977. The effect of severity of coronary artery obstructive disease and the coronary collateral circulation on local histopathologic and electrographic observations in man. *American Journal of Medicine*, *63*, 193–199.

BRANDT, W. T., PARTRIDGE, J. B. and WATTIE, J. W., 1977. Coronary arteriography, method of presentation of the arteriogram report and scoring system. *Clinical Radiology*, *28*, 361–365.

COHEN, M. V., 1978. The functional value of coronary collaterals in myocardial ischaemia and therapeutic approach to enhance collateral flow. *American Heart Journal*, *95*, 396–401.

FLAMENG, W., SCHWARZ, F., HERLEIN, F. and BOEL, A., 1978. Functional significance of coronary collaterals in man. *Basic Research in Cardiology*, *73*, 188–199.

FRICK, M. H., KORHOLA, O., VALLE, M., RIIHIMAKI, E. and WILJASLO, M., 1976. Radiologically detected collaterals and regional myocardial flow responses to ischaemia in ischaemic heart disease. *Annals of Clinical Research*, *8*, 241–247.

HECHT, H. S., AROESTY, J. M., MORKIN, E., LA RALA, P. J. and PAULIN, S., 1975. Role of coronary collateral circulation in the preservation of left ventricular function. *Radiology*, *114*, 305–313.

HELFANT, R. H., BODENHEIMER, M. M. and BANKA, V. S., 1977. Asynergy in coronary heart disease. *Annals of Internal Medicine*, *87*, 475–482.

HELFANT, R. H., KEMP, H. G. and GORLIN, R., 1970. Coronary atherosclerosis, coronary collaterals, and their relation to cardiac function. *Annals of Internal Medicine*, *73*, 189–193.

HELFANT, R. H., VOKONAS, P. S. and GORLIN, R., 1971. Functional importance of the human coronary circulation. *The New England Journal of Medicine*, *284*, 1277–1280.

KNOEBEL, S. B., MCHENRY, P. L., PHILLIPS, J. F. and PAULETTO, F. J., 1972. Coronary collateral circulation and myocardial blood flow reserve. *Circulation*, *46*, 84–93.

LAVINE, P., FILIP, Z., NAJMI, M., KIMBIRIS, D., SEGAL, B. and LINHARD, J. W., 1974. Clinical haemodynamic evaluation of coronary collateral vessels in coronary artery disease. *American Heart Journal*, *87*, 343–349.

LEVIN, D. C., SOS, T. A., LEE, J. G. and BALTAXE, H. A., 1973. Coronary collateral circulation and distal coronary run off. The key factors in preserving myocardial contractility in patients with coronary artery disease. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *119*, 474–483.

MCGREGOR, M., 1975. The coronary collateral circulation. *Circulation*, *52*, 529–530.

SCHAPER, W., FLAMENG, W., WUSTEN, B. and PELMOWSKI, J., 1973. Distribution of coronary collateral flow in normal hearts after coronary artery occlusion. *Advances in Experimental Medical Biology*, *39*, 151–160.

SHAKHOV, B. E., 1978. Coronary bed in aneurysm of left ventricle. *Kardiologia*, *18* (12), 49–53.

1981, *British Journal of Radiology*, *54*, 736–743

The three types of criss-cross heart: a simple rotational anomaly

By *S. M. Tadavarthy, M.D., *A. Formanek, M.D., *W. Castaneda-Zuniga, M.D.,
†J. H. Moller, M.D., ‡J. E. Edwards, M.D. and *K. Amplatz, M.D.

Departments of *Radiology and †Pediatrics, University of Minnesota Hospitals, Minneapolis, Minnesota, and
‡Department of Pathology, Miller Hospital, St. Paul, Minnesota

(*Received August 1980 and in revised form March 1981*)

ABSTRACT

Criss-cross heart is an angiographically confusing malformation where apparent crossing but not mixing of contrast medium is seen at atrioventricular level. The malformation can be understood by a clockwise or counter-clockwise ventricular rotation. In the normal heart or one with complete transposition ventricular rotation is clockwise. With corrected transposition rotation occurs in a counter-clockwise fashion. One case of criss-cross heart with associated corrected transposition and two criss-cross hearts occurring with complete transposition are reported.

Criss-cross heart is a rare congenital malformation which represents a diagnostic challenge to cardiac radiologists and cardiologists.

The term was introduced in order to explain a complex anatomical arrangement of the AV valves and ventricles seen in hearts with transposition (Anderson *et al.*, 1974). The other designations for this type of complex transposition include "mixed laevocardia", "corrected transposition of the great arteries with extreme counter-clockwise torsion of the heart" (Franco-Vazquez *et al.*, 1973), "uncorrected laevotransposition with horizontal ventricular septum" (Guthauer *et al.*, 1976), "inverted ventricles with normal atrioventricular connections" and "transposed great artery connections" (Elliot, 1978). Because of the confusing terminology, we prefer to retain the descriptive term "criss-cross heart" which was also used by Freedom *et al.* (1978).

It is the purpose of this communication to propose a simple concept for this complex malformation by using a rotational theory. Three well documented cases of criss-cross hearts are described.

CASE REPORTS

Case I

Clinical features. The patient was a boy born following a full-term pregnancy and delivery. At birth the Apgar rating was 9. At 24 h of age, he was cyanotic and a cardiac murmur was noted. Lethargy and cyanosis were noted on physical examination at the age of 30 h. The cardiac rate was

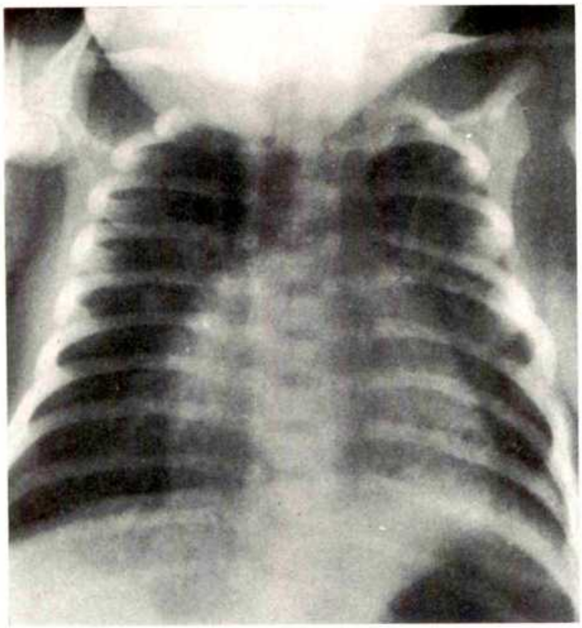


FIG. 1. *Case I.*

PA chest film showing mild cardiomegaly, slightly increased vasculature and narrow mediastinum due to lack of thymic tissue. Left aortic arch.

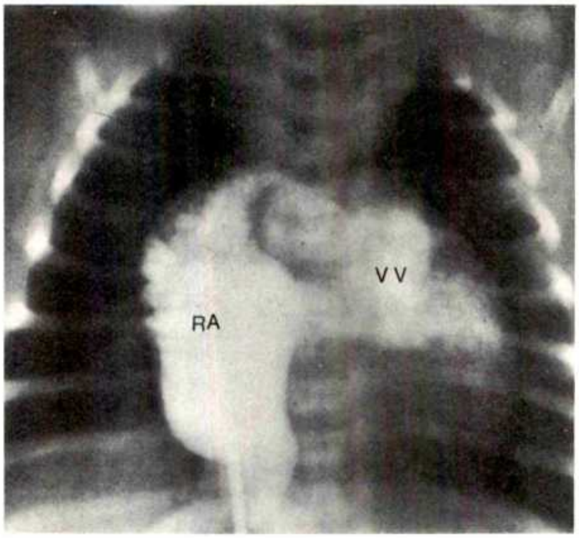
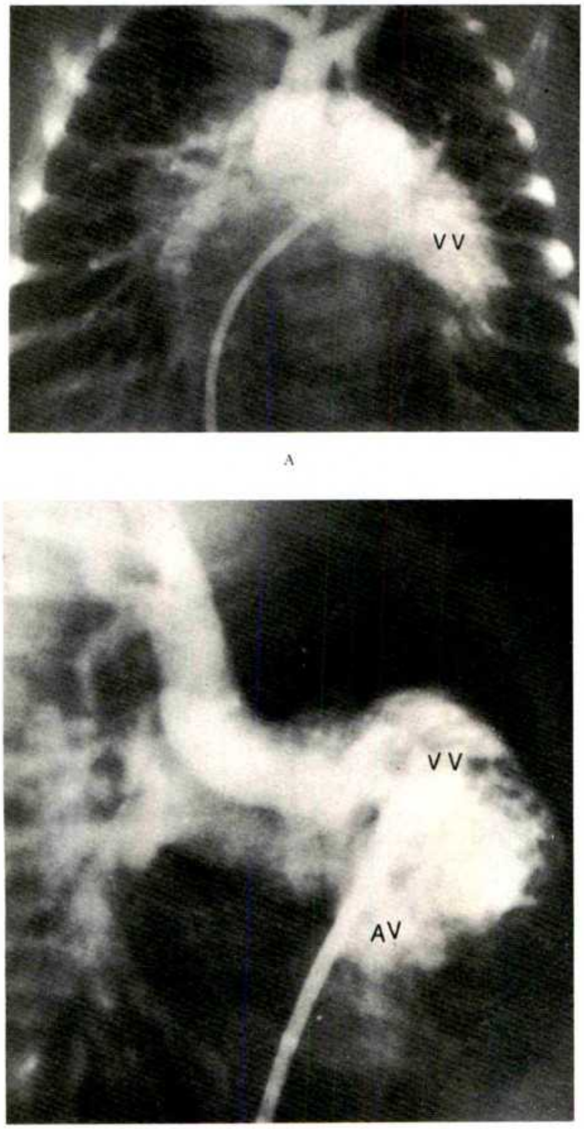


FIG. 2. *Case I.*

Right atriogram (RA) showing an abnormally high tricuspid valve with flow of contrast medium into the venous ventricle (VV) which is located high at the left heart border.

Address for reprints: Kurt Amplatz, M.D., Department of Radiology, University of Minnesota Hospitals, 420 Delaware Street SE, Minneapolis, MN 55455, USA.

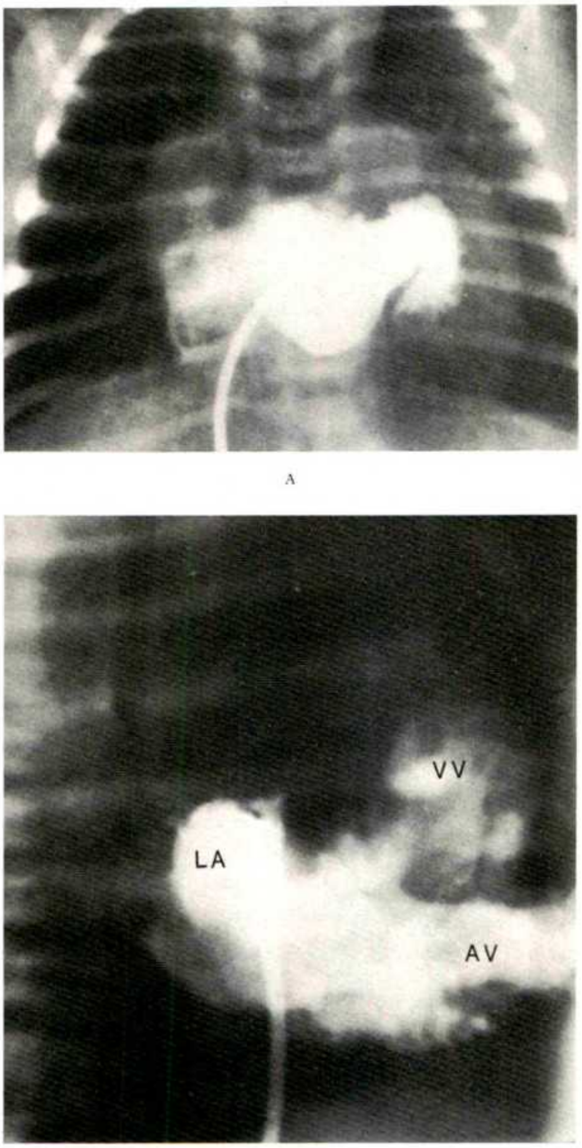


A

B

FIG. 3. *Case 1.*

(A and B) Injection into the venous ventricle (VV) shows trabeculation and an infundibulum indicating an anatomical right ventricle. The aorta arises from this ventricle as in complete transposition. The pulmonary artery arises from the anatomical left ventricle (AV) which fills via ventricular septal defect. The pulmonary artery is transposed.



A

B

FIG. 4. *Case 1.*

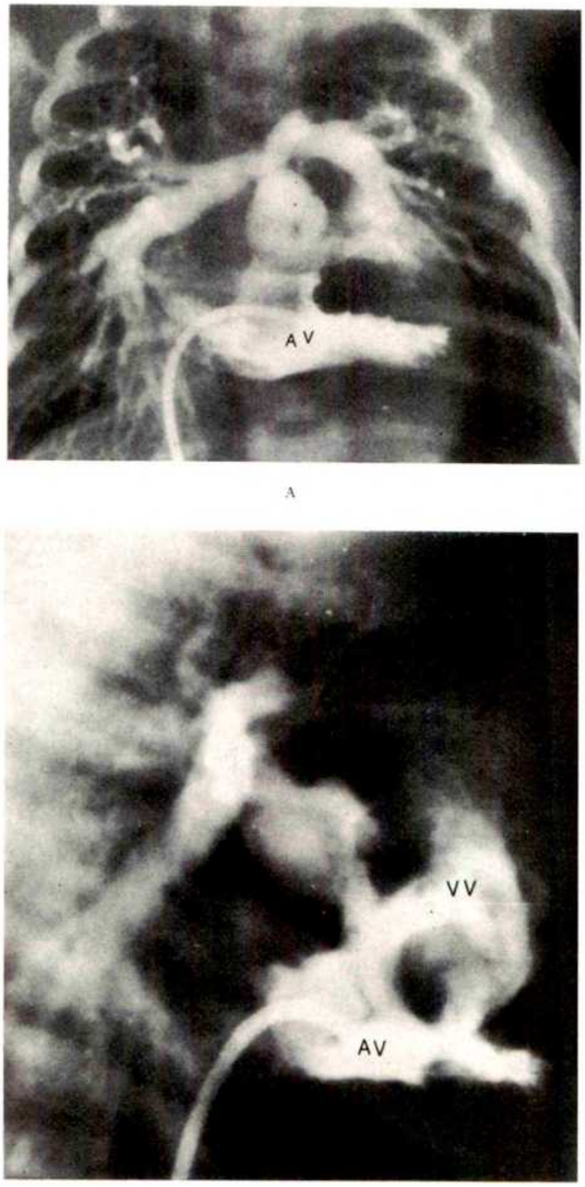
(A and B) Left atrial (LA) injection showing flow of contrast medium into the anatomical left ventricle (AV) which lies inferiorly. The anatomical right ventricle (VV) fills through a ventricular septal defect.

120/min and respiratory rate 60/min. A grade 2/6 mid-systolic murmur was present along the lower left sternal border. The edge of the liver was palpable 3 cm below the right costal margin.

An electrocardiogram was considered normal for age. The thoracic radiograph showed signs of increased pulmonary blood flow and a narrow mediastinum. The cardiac contour was consistent with complete transposition of the great vessels (Fig. 1).

Cardiac catheterization indicated an unusual form of transposition of the great vessels, ventricular septal defect and coarctation of the aorta. A Rashkind procedure (atrial septostomy) was performed, and digitalization was also instituted. The coarctation of the aorta was resected and the ductus arteriosus was ligated when the patient was four days old. Because of persistence of tachypnoea and hepatomegaly, a second catheterization was performed to reassess the cardiac status. Subsequently, a pulmonary arterial band was placed at one month of age, following which the cardiac failure improved. Pneumonia developed and death occurred at the age of four months.

Angiocardiographic findings. A right atriogram showed flow of contrast medium into a ventricle located superiorly and anteriorly along the left heart border (Fig. 2).



A

B

FIG. 5. *Case 1.*

(A and B) AP and lateral views of injection of the smooth walled anatomical left ventricle (AV) shows filling of the pulmonary artery. There is a conus for the pulmonary artery with subpulmonary stenosis. The anatomical right ventricle (VV) fills via ventricular septal defect. On the AP view, the septum is oriented identical to corrected transposition.

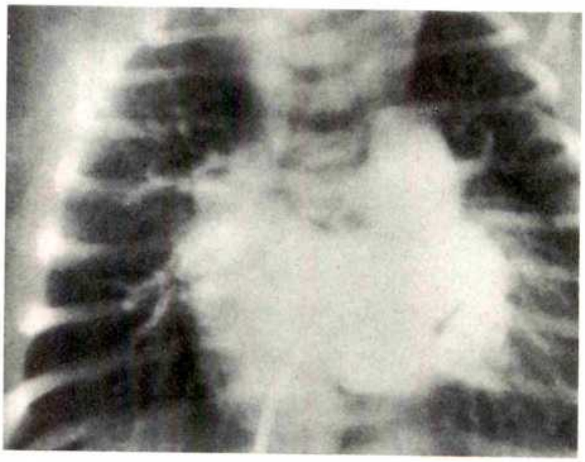


FIG. 6. *Case 1.*

Laevophase showing opacification of the left atrium, left ventricle, and pulmonary artery as in complete transposition of the great vessels.

Selective injection of contrast medium into this ventricle demonstrated both trabeculation and an infundibulum characteristic of an anatomical right ventricle. The aorta originated anteriorly from this ventricle and was located in the mid-line (Fig. 3A). The other ventricle was partially filled through a ventricular septal defect (Fig. 3B). The pulmonary artery was located posteriorly, and the pulmonary valve lay lower than the aortic valve. Coarctation and tubular hypoplasia of the aorta were noted immediately beyond the left subclavian artery, and a left arch was present.

Injection into the left atrium showed this chamber to be normally positioned. The contrast medium passed into a ventricle located posteriorly and inferiorly (Fig. 4A, B). Selective injection into this ventricle showed the smooth interior of an anatomical left ventricle; however, there was clear separation between the mitral valve and the semilunar valve. The ventricular septum was orientated perpendicularly to the anterior chest wall as in some cases of corrected transposition, and separated the left-sided, anterior anatomical right ventricle (venous ventricle) from the right-sided, posterior anatomical left ventricle (arterial ventricle). The pulmonary artery arose from the anatomical left ventricle (arterial ventricle), and there was narrowing below the pulmonary valve (Fig. 5A, B).

In the late phase of this study, reopacification of the left atrium, left ventricle, and pulmonary artery occurred as in complete transposition of the great vessels (Fig. 6).

The angiograms thus showed that the aorta arose anteriorly from an anatomical right ventricle and the pulmonary artery posteriorly from an anatomical left ventricle, and that the passage of the contrast medium was identical to that in complete transposition. The unusual feature was that the anatomical right ventricle lay to the left of the anatomical left ventricle so that the venous inflow to the ventricles appeared to cross.

Pathological findings. The heart was enlarged, and the apex pointed to the left side. The great vessels were transposed, and the aorta lay toward the right and anteriorly to the pulmonary trunk. The ascending aorta pointed toward the right (D-transposition). *In situ* the ventricular septum was positioned in a diagonal fashion so that the anatomical right ventricle occupied a left superior position and the anatomical left ventricle a right inferior position. By counterclockwise rotation, the specimen was almost identical to a regular D-transposition (Fig. 7).

The anatomical right atrium lay to the right of the anatomical left atrium and received the venae cavae and coronary sinus. The aorta arose from the conus of the right ventricle. Two ventricular septal defects were present, each muscular.

The left atrium received the pulmonary veins and led through the mitral valve into the anatomical left ventricle from which arose a pulmonary artery with a bicuspid valve.

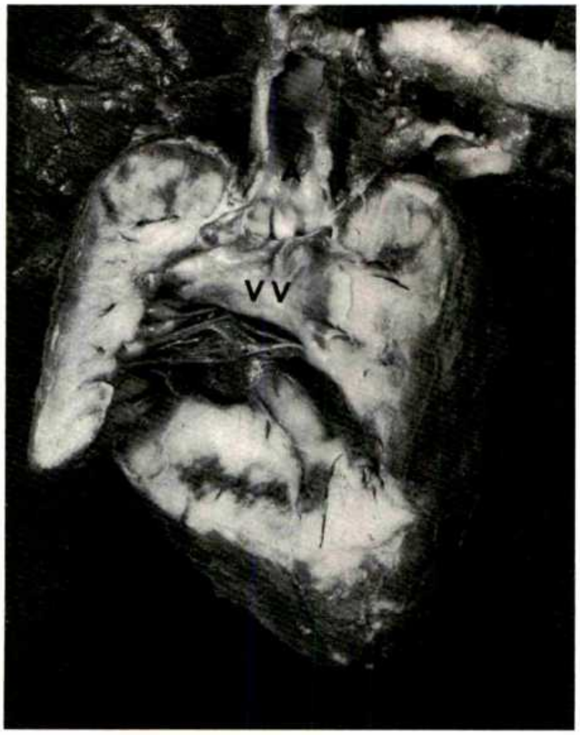


FIG. 7. *Case 1.*
Interior of anatomical right ventricle (VV) and aorta (A). The heart has been rotated in counter-clockwise fashion converting the angiographically demonstrated criss-cross heart into a regular transposition.

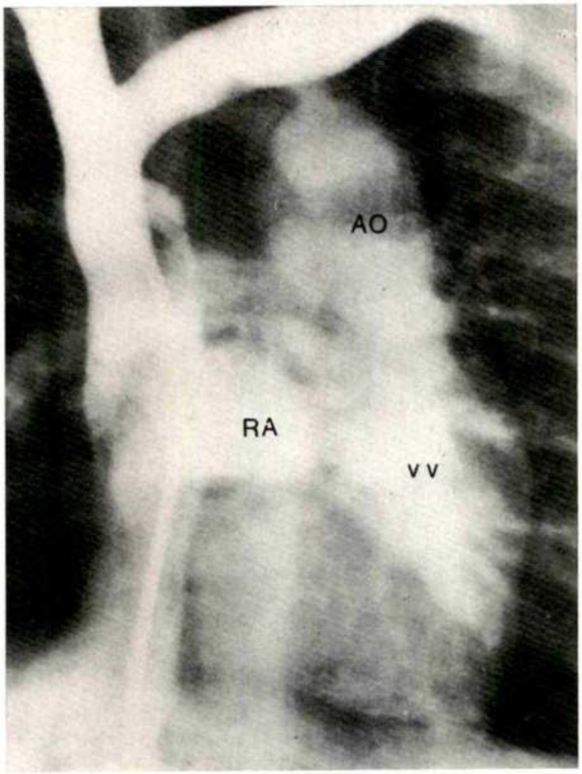


FIG. 8. *Case 2.*
Right atriogram shows reflux of contrast medium into the superior vena cava and inferior vena cava. The right atrium (RA) is small and located abnormally high. The tricuspid valve is in abnormal high location; and there is filling of a ventricle (VV) which occupies the left upper heart border, and there is filling of the aorta (AO) as in complete transposition.

A column of muscle separated the pulmonary and mitral valves, yielding a left ventricular conus and subpulmonary stenosis.

Case 2

Clinical features. A ten-month-old cyanotic male infant was noted to have an elevated haemoglobin value and a cardiac murmur. Physical examination revealed a moderately cyanotic infant with equal blood pressures in the upper and lower extremities. The first cardiac sound was normal and the second sound was loud and single. A grade 2/6 systolic ejection murmur was present along the left sternal border and in the "pulmonary area". The liver was palpable 2 cm below the right costal margin.

The electrocardiogram showed normal P waves and PR interval. The QRS axis was +135°. In each of the precordial leads there was an RS pattern. The thoracic radiographs showed normal pulmonary vascular markings and normal cardiac size. The haemoglobin concentration of the blood was 17.2 g/100 ml and haematocrit was 55%. Cardiac catheterization showed that both ventricles had identical systolic pressures. The pulmonary arterial pressure was not recorded. Atrial pressures were identical. Oximetry data indicated a right-to-left shunt at the atrial level and a left-to-right shunt at the ventricular level.

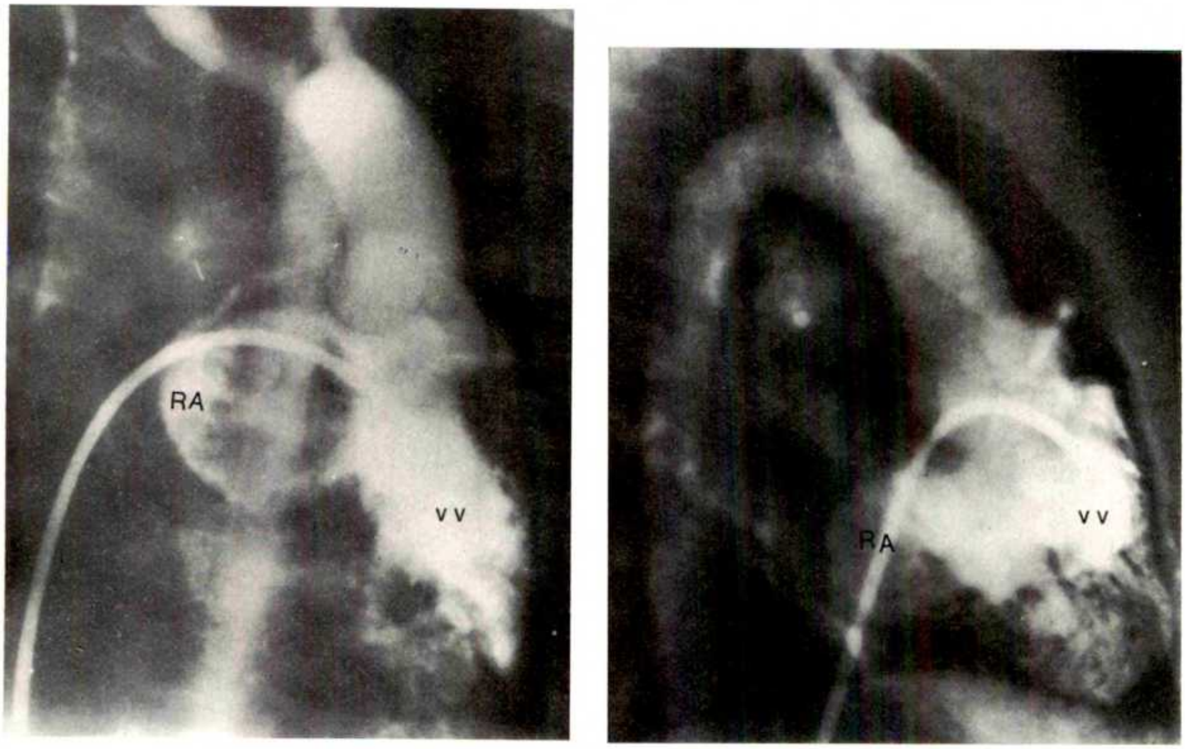
Angiocardiographic findings. A selective right atriogram showed a high position of the right atrium and filling of a ventricle which was located at the left superior heart border (Fig. 8). Injection of contrast medium into this ventricle (Fig. 9A, B) showed marked trabeculation and an infundibulum. The aorta arose from this ventricle and was located anteriorly and to the left similar to corrected transposition. A left atriogram showed the left atrium to be small (Fig. 10) and connected to a ventricle lying posterio-inferiorly. Two papillary muscles were present indicating an anatomical left ventricle. The pulmonary artery arose from this ventricle and was located posteriorly to the aorta as in complete transposition.

Case 3

Clinical features. A baby girl was admitted at two months of age with a diagnosis of congestive heart failure and was treated with digitalis. At ten months of age the child was cyanotic with slow weight gain, remaining below the fifth percentile for her age. There was a systolic thrill at the left sternal border and a loud systolic murmur at the pulmonary area. Cardiac catheterization was undertaken to define the anatomical lesions.

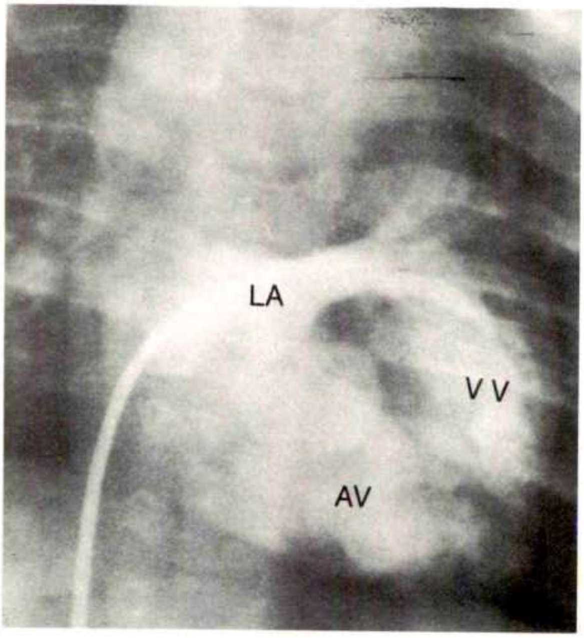
Angiocardiographic findings. The first ventriculogram demonstrated reflux of contrast medium into the right atrium (Fig. 11A, B). This ventricle was located posteriorly and to the left, connected to a pulmonary artery as in corrected transposition. It was smooth-walled, had two papillary muscles, and no infundibulum as in an anatomical left ventricle. There was opacification of the other ventricle and the aorta from a right-to-left shunt through a ventricular septal defect. Both great vessels were clearly transposed. The flow of contrast medium from the right atrium through the right AV valve into the anatomical left ventricle was confirmed haemodynamically by cardiac catheterization.

Selective injection of contrast medium into the other ventricle which lay anteriorly and to the right showed an



A FIG. 9. *Case 2.* B

(A and B) Injection into the left-sided anatomical right ventricle (VV) showing reflux into the right atrium (RA) and opacification of the aorta as in complete transposition. Position of the aorta identical to corrected transposition.



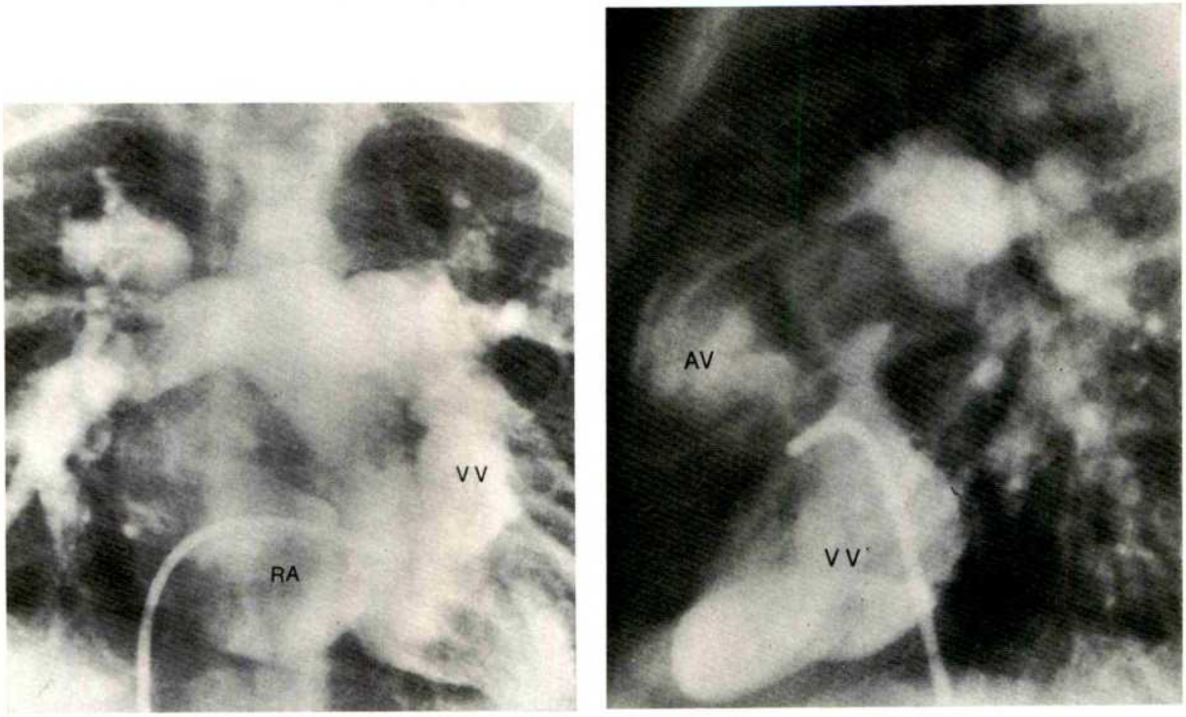
anatomical right ventricle. At cardiac catheterization, it was confirmed that this ventricle received pulmonary venous blood, being 94% saturated. The left ventricle (venous ventricle) and pulmonary artery were faintly opacified via ventricular septal defect (Fig. 12A, B). The aortic valve was higher than the pulmonary valve indicating that it was connected to an anatomical right ventricle with an infundibulum. Thus, all features of corrected transposition were present except for the anomalous position of the ventricles resulting in apparent crossing of the blood stream at the AV valve level.

DISCUSSION

The three reported cases are angiographically and haemodynamically well documented. Cases 1 and 2 have the haemodynamic features of complete transposition; Case 3 is physiologically normal but has transposed great vessels, as in corrected transposition. Case 2 has one angiographic characteristic of corrected transposition, namely the aorta in apparent L position. Case 3 again does not look like the usual corrected transposition in that the position of the aorta resembles angiographically D-transposition.

FIG. 10. *Case 2.*

Left atriogram showing reflux into left pulmonary veins and filling of the right-sided anatomical left ventricle (AV). There is also filling of the anatomical right ventricle (VV) through a ventricular septal defect. LA = left atrium.

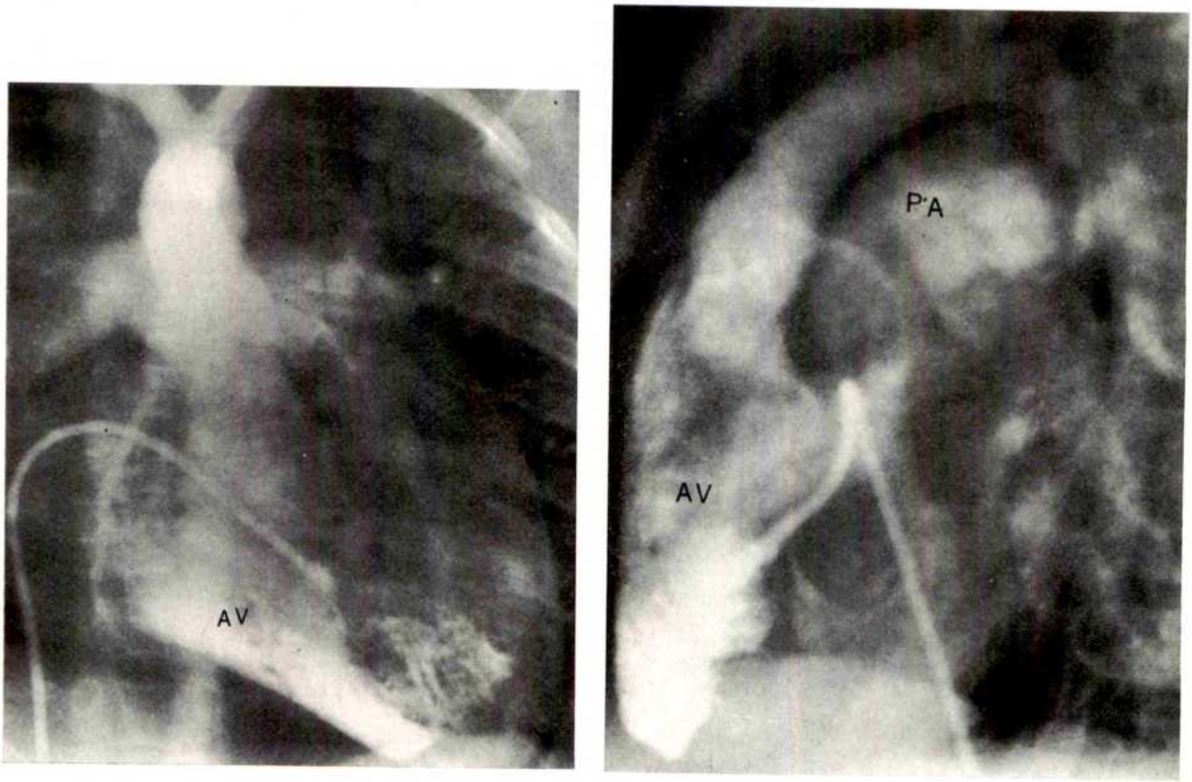


A FIG. 11. *Case 3.* B

(A) Injection into the left-sided anatomical right ventricle (VV) shows reflux into and therefore connection to the right atrium (RA). Dense filling of the pulmonary artery. Low position of the pulmonary valve indicating absent infundibulum as in an anatomical left ventricle.

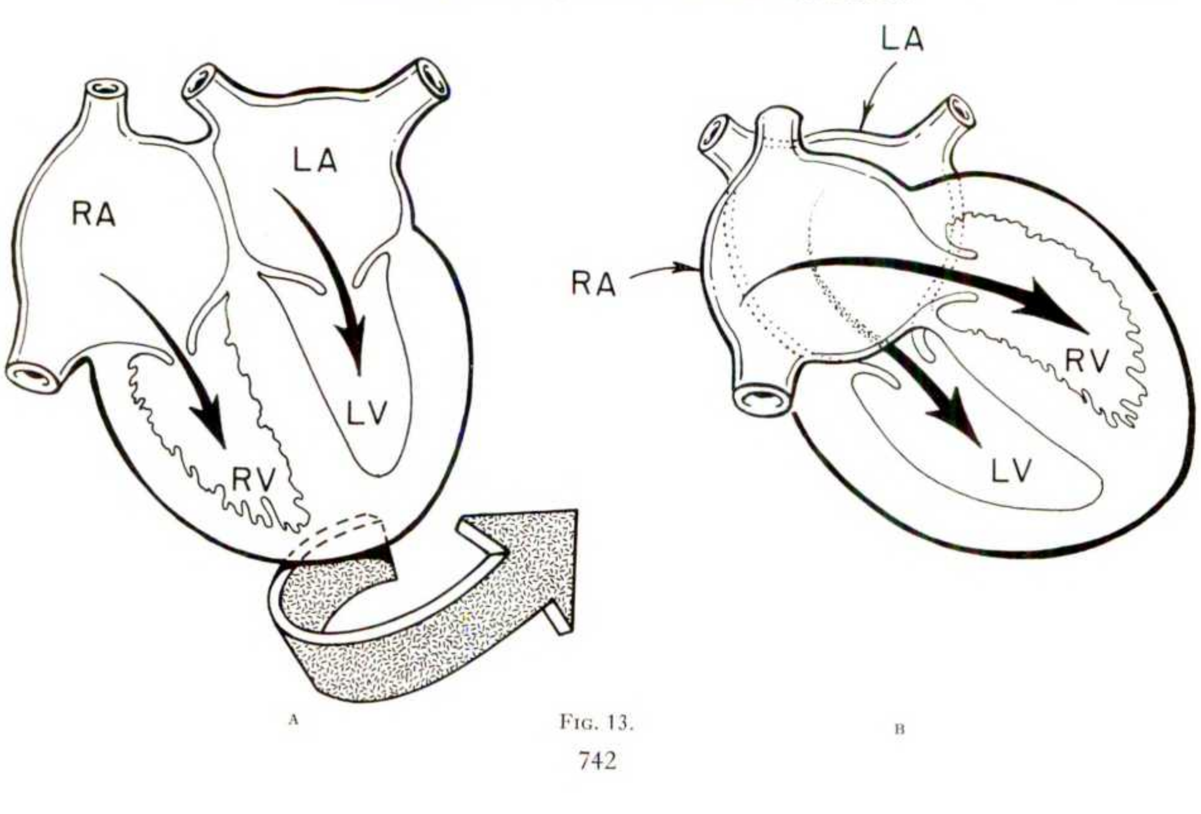
(B) Filling of right-sided anatomical left ventricle (AV) via ventricular septal defect. Pulmonary artery in posterior position as in transposition. VV = anatomical right ventricle.

The malformation can be readily understood if one considers it as a rotational anomaly of the ventricles. If a heart with complete transposition is rotated in clockwise fashion (Fig. 13B), the trabeculated right ventricle will occupy an abnormally high, left superior-anterior position; and the left ventricle will be located lower and medially. Thus, both ventricles have a similar orientation as seen in corrected transposition; and the septum may be seen end on, on AP views. Obviously the marked rotation of the heart involves also rotation of the AV and semilunar valves. Consequently, the right AV valve will be positioned high and to the left; and the left AV valve will occupy a more medial and lower position. The venous blood, therefore, will stream from right-to-left and the pulmonary venous blood stream from left to right. Venous inflows are "crossed", consistent with the original definition of "criss-cross" heart. With rotation of the ventricles there is also rotation of the great vessels. The aorta arising from the venous ventricle may be located to the left of the pulmonary artery, thus stimulating "corrected transposition" (Case 2). The correct diagnosis in the Cases 1 and 2 was "complete transposition of the great vessels with ventricular rotation" or "criss-cross heart and complete transposition". Case 1 was confirmed pathologically. By rotating the specimen in counter-clockwise fashion, the pathologist was converting the criss-cross heart into a regular D-transposition (Fig. 7). Case 3 can be readily understood if a heart with corrected transposition is rotated in counter-clockwise fashion. Now the right AV value (bicuspid) will occupy a position more to the left. On the other hand, the left AV valve will assume a more medial position. The flow of blood through the AV valves is not altered by this rotation, but "crossing" of contrast medium is seen angiographically at AV valve level conforming with the definition of "criss-cross heart" (Fig. 14A, B). The right-to-left relationship of the great vessels is altered by this rotation and the classical position of the aorta is lost. The correct diagnosis can therefore be made by keeping this rotational anomaly in mind and disregarding the right-to-left relationship of the great vessels and ventricles. The third case, therefore, is an example of corrected transposition of the great vessels with counter-clockwise ventricular rotation or a criss-cross heart occurring in corrected transposition.



A FIG. 12. *Case 3.* B

(A and B) AP and lateral views showing anatomical right ventricle (AV) which opacifies a transposed aorta. Transposed pulmonary artery (PA) opacified via ventricular septal defect.



A FIG. 13. B

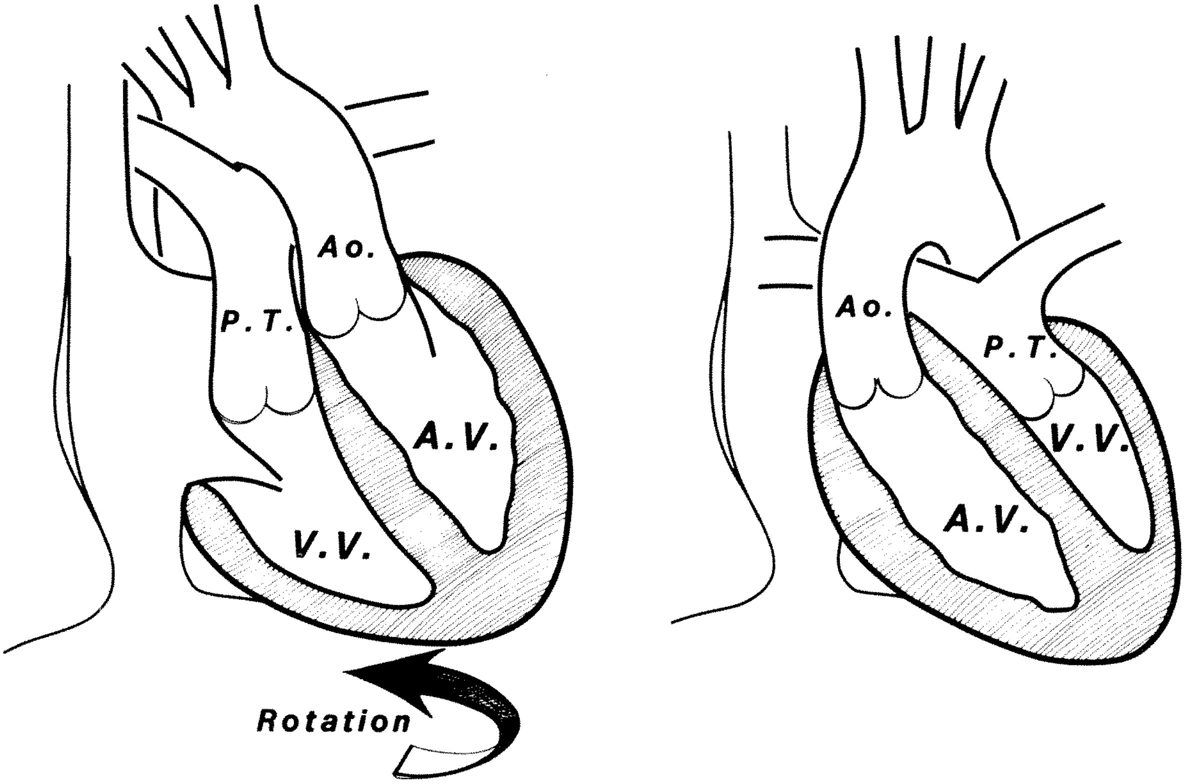


FIG. 14.

Recently Sato *et al.* (1978) described a criss-cross heart in a normal heart except for a small ventricular septal defect. Clockwise rotation placed the right ventricle along the left upper heart border, thus resulting in apparent crossing of blood at the atrial level. This case, therefore, represents a clockwise rotational anomaly in a normal heart.

It is interesting to note that pathologists are less impressed with criss-cross hearts than angiographers. If the heart is removed from the body it can be rotated, making the angiographic criss-cross feature disappear (Fig. 7). The pathologist may, therefore, overlook the diagnosis.

SUMMARY AND CONCLUSION

(1) In criss-cross hearts apparent crossing but not mixing of blood flow occurs at atrioventricular level. (2) Criss-cross hearts may be seen with complete transposition, corrected transposition, and normal hearts (the three criss-cross hearts). (3) The angiographic appearance of crossing is produced by rotation of the heart along the long axis of the ventricles. The rotation is clockwise (seen from below) in hearts with atrioventricular concordance and counter-clockwise in hearts with atrioventricular discordance. (4) In order to establish the correct diagnosis, angiograms should be analysed first according to the haemodynamic features since some of the anatomical characteristics may be lost or altered. (5) The clinical, haemodynamic, angiographic and pathological features of two criss-cross hearts occurring in complete transposition and one criss-cross heart associated with corrected transposition are described.

REFERENCES

ANDERSON, R. H., SHINEBOURNE, E. A. and GERLIS, L. M., 1974. Criss-cross atrioventricular relationships producing paradoxical atrioventricular concordance or discordance. Their significance to nomenclature of congenital heart disease. *Circulation, 50,* 176–180.

ELLIOT, L. P., 1978. Angiocardiographic plain film approach to complex congenital heart disease, classification and simplified nomenclature. *Current Problems of Cardiology, 3* (3) (Yearbook Medical Publishers, Chicago), p. 27.

FRANCO-VAZQUEZ, J. S., PEREZ-TREVINO, D. and GAXIOLA, A., 1973. Corrected transposition of the great arteries with extreme counter-clockwise torsion of the heart. *Acta Cardiologica* (Brussels), *28,* 636–643.

FREEDOM, R. M., CULHAM, G. and ROWE, R., 1978. The criss-cross and superioinferior ventricular heart: an angiographic study. *American Journal of Cardiology, 42,* 620–628.

GUTHANER, D., HIGGINS, C. B., SILVERMAN, J. F., HAYDEN, W. G. and WEXLER, L., 1976. An unusual form of the transposition complex. Uncorrected levo-transposition with horizontal ventricular septum: report of two cases. *Circulation, 53,* 190–195.

SATO, K., OHARA, S., TSUKAGUCHI, I., YASUE, K., NAKADA, T., TAMAI, M., KOBAYASHI, Y. and KUZUKA, T., 1978. A criss-cross heart with concordant atrioventriculoarterial connections. Report of case. *Circulation, 57,* 396–400.

1981, *British Journal of Radiology*, *54*, 744-753

Computerized tomography versus angiography in the staging of malignant renal neoplasm

By P. Probst, H. M. Hoogewoud, M. Haertel, E. Zingg and W. A. Fuchs

Department of Diagnostic Radiology and Department of Urology, University Hospital, Bern, Switzerland

(*Received September 1980 and in revised form April 1981*)

ABSTRACT

A comparative diagnostic study was carried out on 40 patients with pathologically proven renal malignancies which were staged both by angiography and CT. CT is more accurate than angiography for the detection of both perirenal and pararenal extension of the primary tumour (T-staging), and angiography is only slightly superior to CT in the evaluation of intravascular extension of the malignancy. The diagnostic performance of CT is clearly superior to angiography in detecting malignant lymphatic spread (L-staging) and distant metastases (M-staging). CT is, therefore, becoming the primary diagnostic approach for the staging of renal malignant tumours.

Renal angiography is currently regarded as the final diagnostic step in the preoperative assessment of patients with a renal malignant mass lesion, because in most cases angiographic examination can define both the nature and extent of the lesion and also demonstrate the patency or obliteration of the renal vein. However, CT appears to offer a non-invasive method of obtaining similar or even better information. The present investigation compares the diagnostic value of angiography and CT in staging renal malignancies.

MATERIAL AND METHODS

Forty patients (19 males, 21 females), 12 to 78 years old with a mean age of 55.9 years, each underwent angiography and CT within three days. In approximately one-third of the cases the CT was performed immediately after the angiography, which included a midstream aortogram, a selective renal study in the A-P and oblique views and an inferior vena cavogram. Renal phlebograms were performed if the condition of the renal vein remained in doubt.

CT examination with a fan beam five-second scanner* included a native and contrast (ioxithalamate† 1 ml/kg=380 mg iodine/kg) enhanced study of the abdomen with a series of 8 mm sections of the renal region, and usually 16 mm sections of other parts of the abdomen.

The radiological findings were compared with the surgical and pathological reports. In two patients with local inoperable tumours, and in one with multiple distant metastases, a positive cytology report after fine-needle biopsy was available; in one patient, who died before treatment, the autopsy results were available. The morphological features used to interpret the angiograms and CT examinations and stage the renal malignancies are listed in Table I. The

TABLE I

MORPHOLOGICAL CRITERIA FOR THE INTERPRETATION OF ANGIOGRAPHY AND CT IN STAGING RENAL MALIGNANCIES

	Angiography	CT
Perirenal infiltration	Capsular and/or retroperitoneal hypertrophied collaterals	Obliteration of perirenal fat plane. Thickening of perirenal fascia
Pararenal infiltration	Parietal and visceral hypertrophied collaterals	Obliteration of contour and fat planes towards adjacent organs or gut Direct invasion of organs and structures
Renal vein involvement	Striated vessel pattern Lack of opacification plus retroperitoneal collaterals Constant filling defects during phlebogram	Increase of venous diameter Abrupt change of venous calibre Retroperitoneal collaterals
IVC involvement	Striated vessel pattern Constant filling defects Collaterals	Intraluminal areas of decreased density Lack of enhancement (pedal injection) Collaterals
Lymph node involvement	Extrarenal focal pathological vessel and/or tumour blush	Enlarged nodular element

---

*Somatom (Siemens, Erlangen, Germany).

†Telebrix 38 (Guerbet, Aulnay-sous-Bois, France).

spread of the tumour into the subcapsular, perirenal and pararenal spaces was estimated.

RESULTS

Out of the 40 renal malignancies (Table II), 37 were primary renal tumours, two were retroperitoneal sarcomas probably originating from the renal capsule and in one case metastases from adenocarcinoma of the lung were present.

Tumour staging by angiography

In 15 renal malignancies (renal cell carcinoma eight, transitional cell carcinoma five, nephroblastoma one, metastases one) there was no pathological evidence of perirenal tumour spread. The angiogram correctly diagnosed the tumour as intrarenal, that is, confined within the renal capsule, in 14 cases (Table III). The smallest of these tumours, a renal cell carcinoma of 2.5 cm diameter, showed a

TABLE II

SPECIFIC PATHOLOGY OF 40 MALIGNANT RENAL MASS LESIONS

Pathology*	$N = 40$
Renal cell carcinoma	29
Transitional cell carcinoma	6
Nephroblastoma	2
Sarcoma	2
Metastasis	1

*The specimens were examined at the department of Pathology, University of Bern.

TABLE III

RESULTS OF TUMOUR STAGING BY ANGIOGRAPHY. CORRECT DIAGNOSIS ARE IN BOLD TYPE WITH OVERSTAGED CASES TO THE RIGHT, UNDERSTAGED TO THE LEFT

Pathology	Angiographic staging		
	Intrarenal	Perirenal	Pararenal
Intrarenal = 15	**14**	1	—
Perirenal = 20	8	**11**	1
Pararenal = 5	—	2	**3**

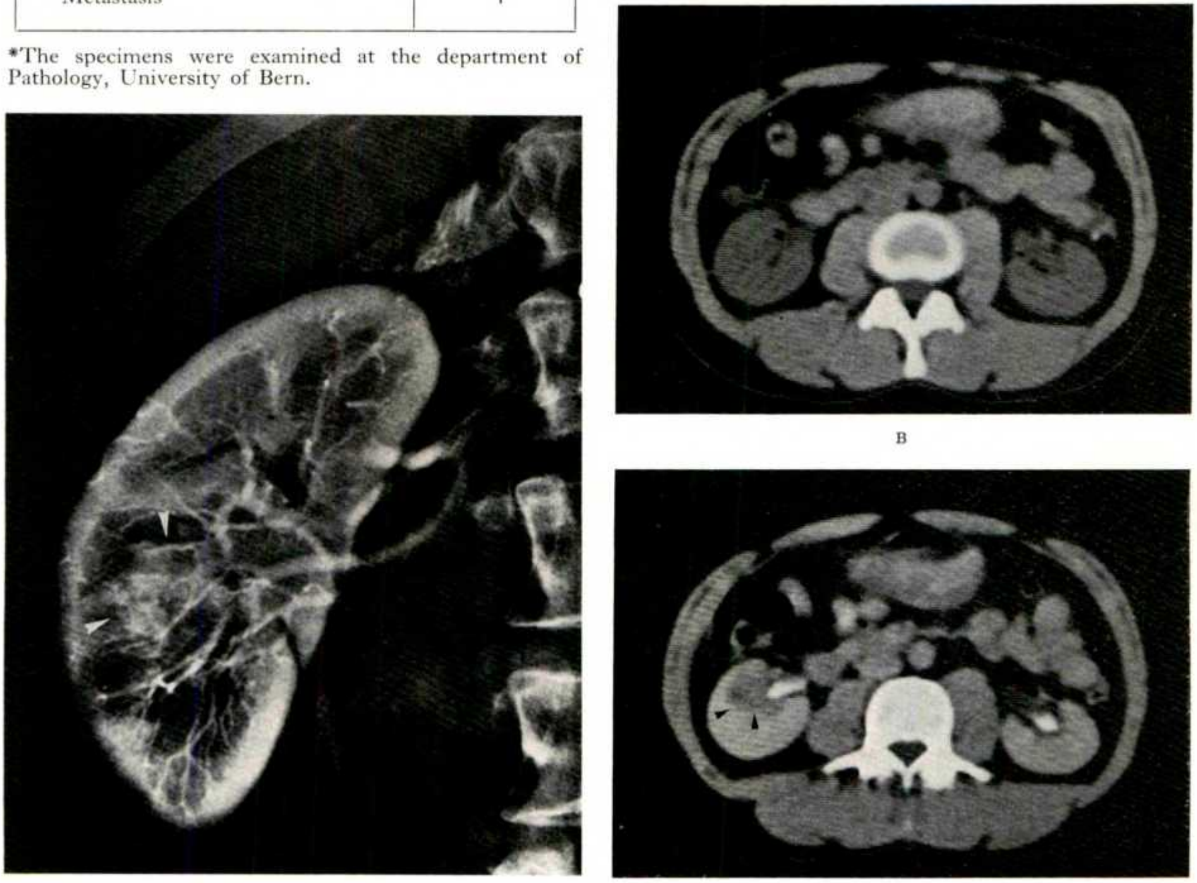
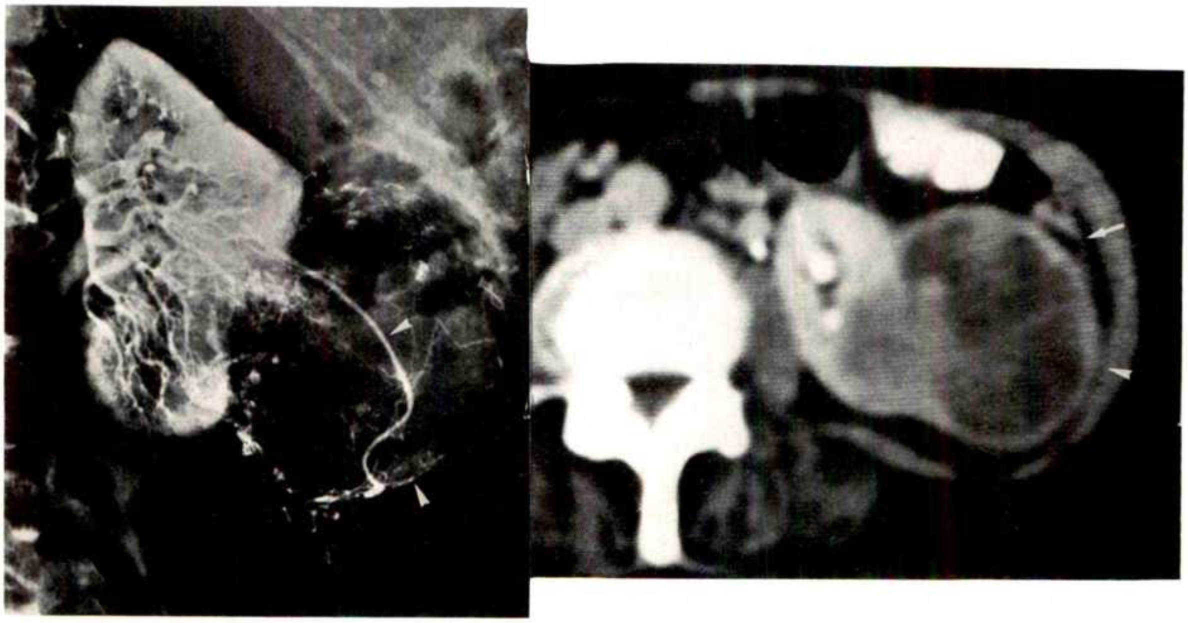


FIG. 1.

Intrarenal localization. (A) Angiography: small irregular medullary area of hyperopacification with pathological vessels. (B) CT: discrete hypodense area impinging on the renal sinus. (C) CT: hypodense opacification of the lesion during enhancement.



A FIG. 2. B

Perirenal tumour extension. (A) Angiography: the tumour is partly nourished by a hypertrophied capsular artery. (B) CT: thickening of renal fascia and obliteration of adjacent fat.

minimal area with pathological vessels and indistinct tumour blush (Fig. 1). The largest protruded 7 cm out of the renal surface with the capsule still intact. In one case perirenal invasion was suspected because of extra-renal blood supply of the malignant mass lesion.

Twenty patients (renal cell carcinoma 16, nephroblastoma one, transitional cell carcinoma one, sarcoma two) showed pathological evidence of perirenal extension beyond the renal capsule but were confined within the renal fascia (Fig. 2). In only 11 cases was this shown by angiography; in eight cases the tumour was thought to be localized within the renal capsule and in one case with saprophytic arterial supply in the splenic hilum, pararenal spread was discussed but not confirmed at the time of surgery. Of five proven pararenal tumour spreads (all renal cell carcinomas) three were diagnosed correctly (Fig. 3). Angiography failed to discern invasion of the pancreas and mesocolon in one case and of the psoas muscle in another. Thus, tumour staging by angiography was correct in 28 of 40 cases, understaged in ten and overstaged in two (Table III).

Tumour staging by CT

Of the 15 malignancies confined within the renal capsule, two were wrongly thought to have spread into the perirenal, and one into the pararenal space (Table IV) because CT could not separate the contours of the renal mass lesion from the surrounding tissue structures. In the latter case, the fat plane between the pancreatic body and a left-sided adenocarcinoma (adult nephroblastoma) in a 31-year-old man could not be identified on neighbouring sections.

TABLE IV

THE RESULTS OF TUMOUR STAGING BY CT. NUMBERS CORRECTLY DIAGNOSED SHOWN IN BOLD TYPE, WITH OVERSTAGED CASES TO THE RIGHT, UNDERSTAGED TO THE LEFT

Pathology	CT staging		
	Intrarenal	Perirenal	Pararenal
Intrarenal = 15	**12**	2	1
Perirenal = 20	—	**19**	1
Pararenal = 5	—	—	**5**

Nineteen of 20 tumours with perirenal spread were diagnosed correctly (Fig. 2). In one case no fat plane was seen towards the colon and consequently pararenal spread was postulated, but disproved by surgery. All five cases of pararenal spread were diagnosed correctly (two paravertebral muscle, one pancreas and transverse mesocolon, one liver, one

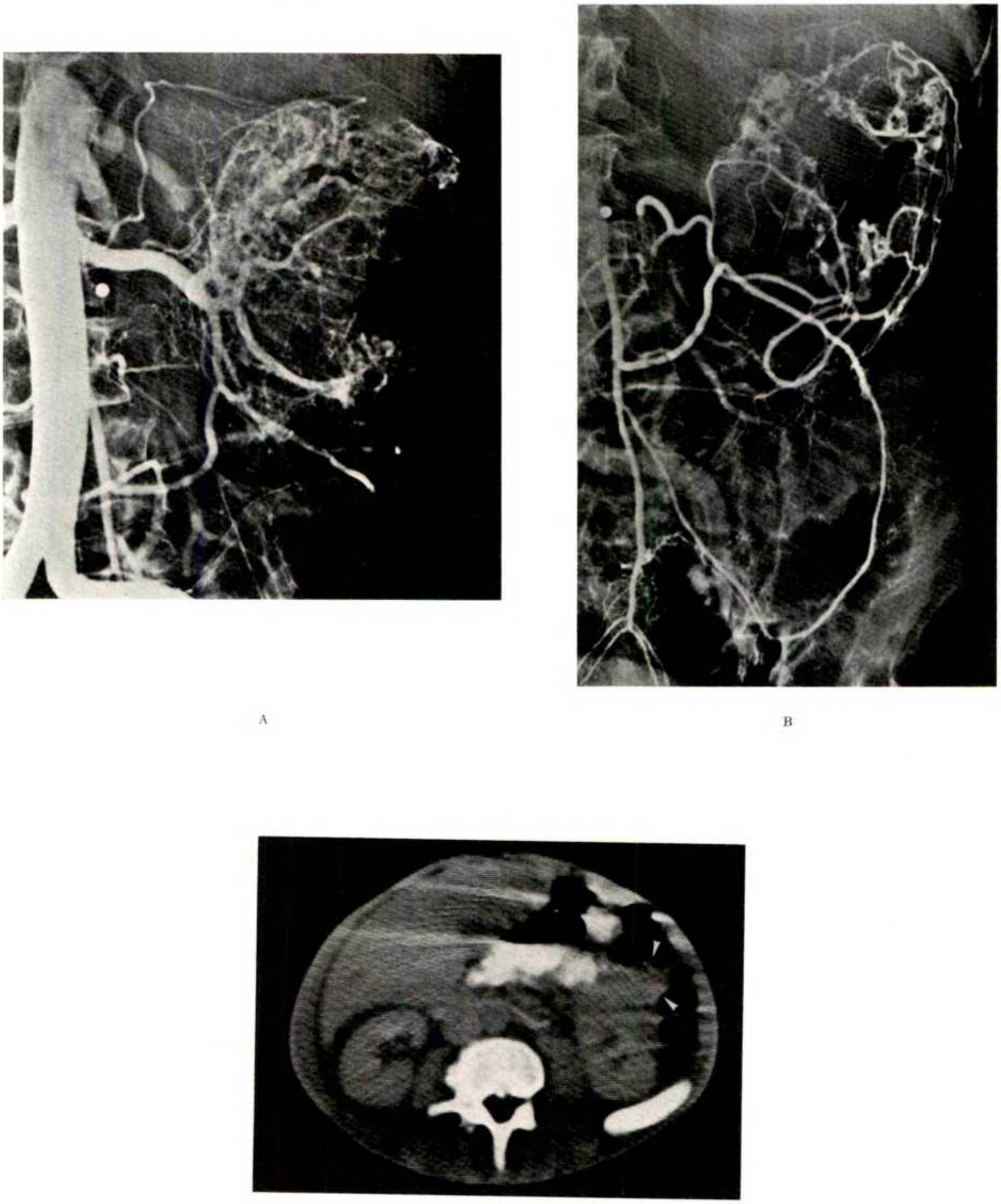


FIG. 3.

Pararenal tumour extension. (A) Angiography: the tumour replaces the whole kidney. Hypertrophied capsular artery. (B) Angiography: parts of the tumour are nourished via the hypertrophied IMA. (C) CT: tumour extension towards the splenic flexure with obliteration of fat plane.

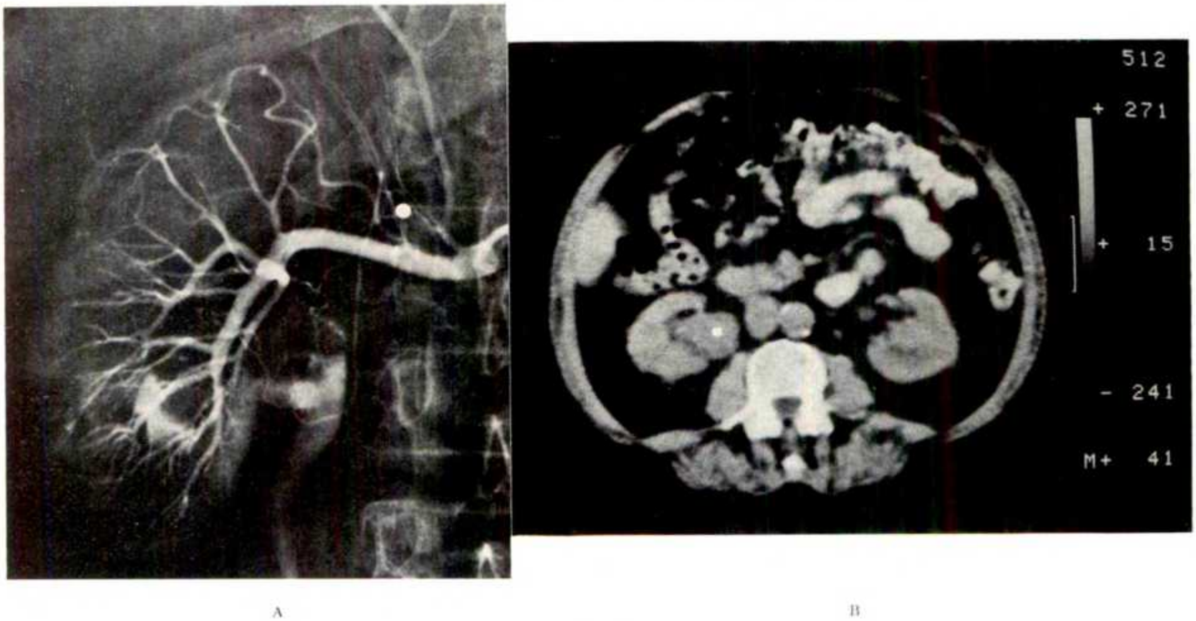


FIG. 4.

Transitional cell carcinoma. (A) Angiography: encasement of small pelvic arteries, minute pathologic vessels and filling defects of the pyelon. (B) CT: increased density and enlargement of the pyelon with partial replacement of hilar fat.

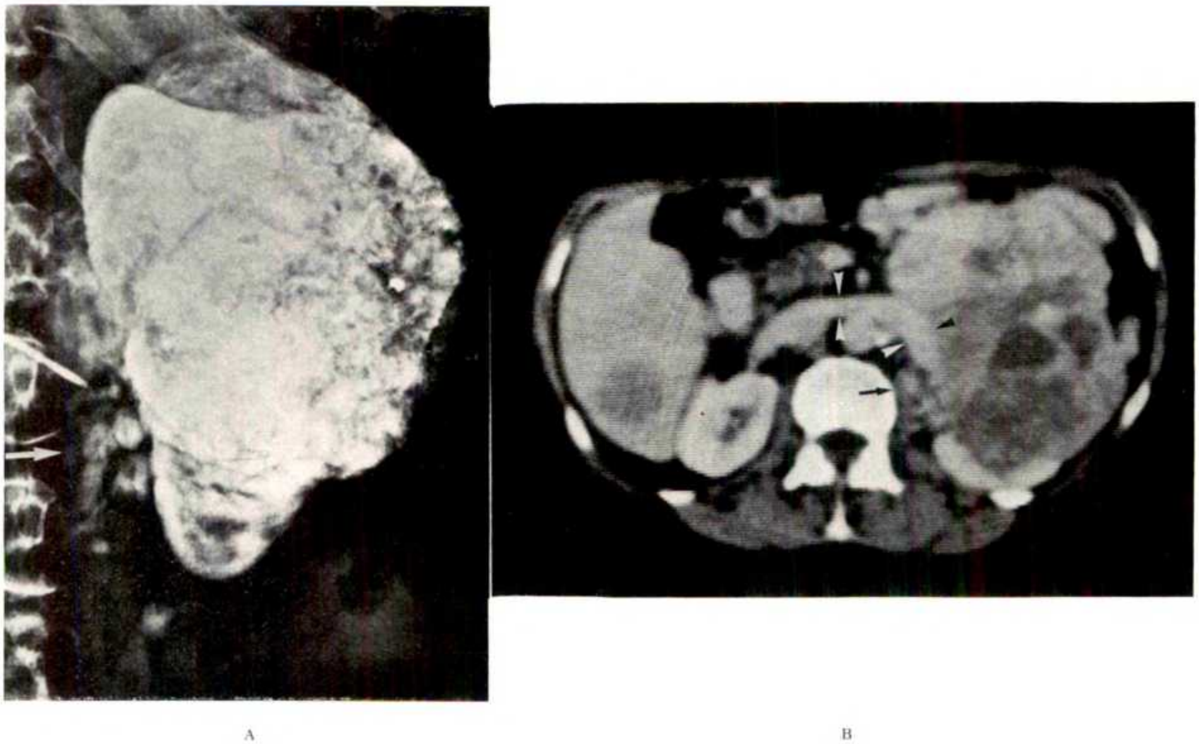


FIG. 5.

Renal vein involvement. (A) Angiography, high volume study (30cc): opacification of retroperitoneal collaterals. (B) CT: increase of renal vein diameter plus retroperitoneal collaterals. Hypodense hepatic lesion (haemangioma).

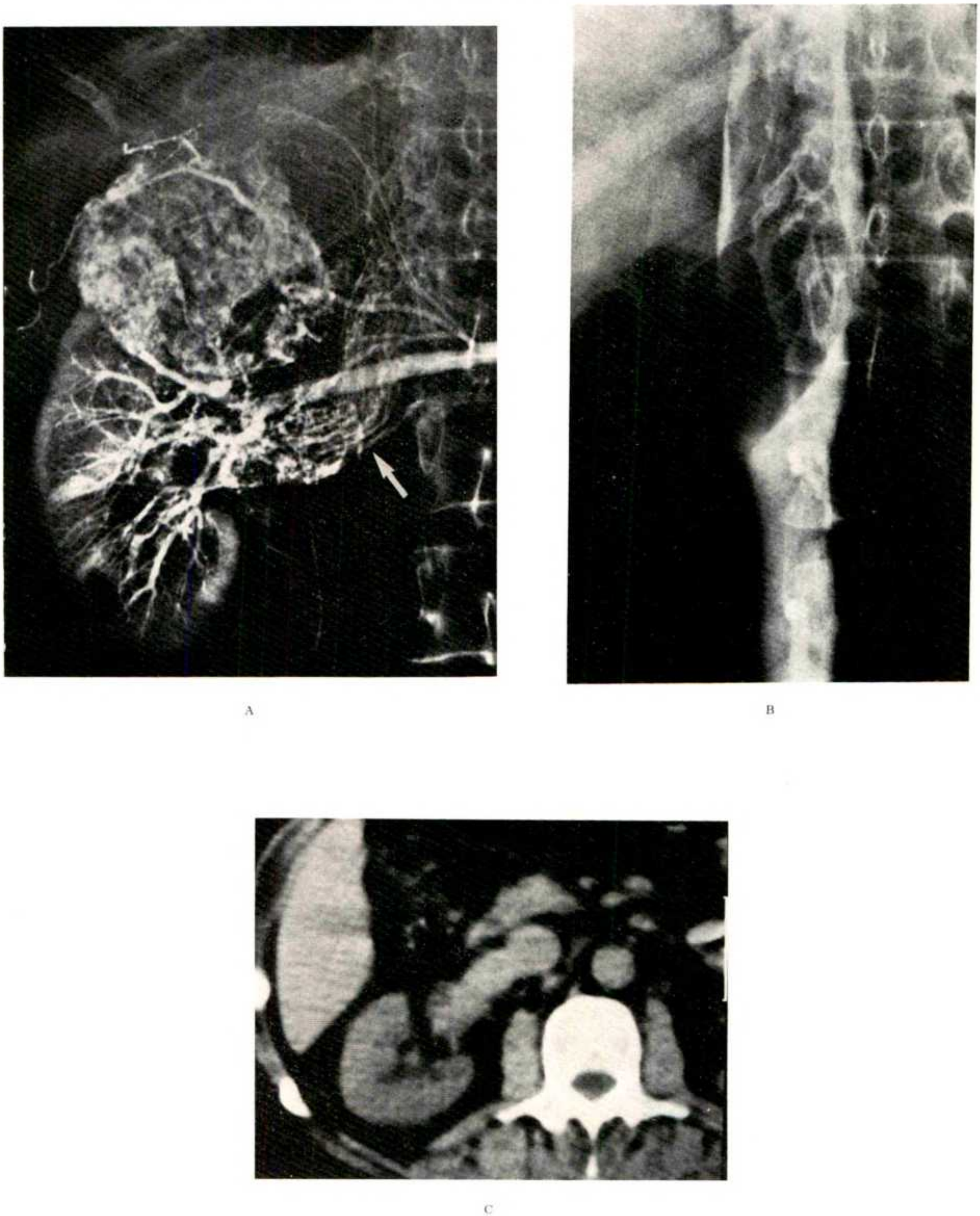


FIG. 6.

Involvement of IVC. (A) Angiography: striated vessel pattern in the area of the renal pedicle and IVC. (B) Cavogram: constant filling defect broadly based at the level of the renal vein orifice. (C) CT: broadening of the renal vein, outbulging of its contour, decreased density in the lumen of the cava.

descending colon) (Fig. 3). Thus, CT allowed correct tumour staging in 36 cases out of 40; four lesions were overstaged (Table IV).

The lesions of transitional cell carcinoma were demonstrated by both angiography (Fig. 4A) and CT (Fig. 4B) in all five cases. Due to the typical paucity of tumour vascularity they were, however, more readily identified by CT by the increase of density (25–35 HU) of the renal pelvis and replacement of hilar fat.

Vascular involvement

Surgical pathology showed the renal vein to be occluded by tumour invasion in seven cases; angiography gave the correct diagnosis in seven/seven cases, CT in six/seven (Fig. 5). In the false negative case, the left renal vein was occluded only in the renal hilum, which was diagnosed by a phlebogram. There was one false positive case for both angiography and CT, in which the renal vein was merely functionally occluded by the pressure of an extra-vascular tumour mass.

Of four cases of tumour extension into the inferior vena cava, all were diagnosed correctly by angiography, only three by CT (Fig. 6). The false negative case was a right-sided malignancy with only a small caval tumour thrombus. A false positive diagnosis was made by CT because the tumour extended into the area of the vena cava, obliterating the vessel contour; angiography proved that the vein was compressed but not infiltrated.

Lymph node staging

Nodular soft tissue structures of more than 1.5 cm in diameter were depicted by CT within the region of the hilum, along the renal pedicle (Fig. 7) or near the inferior vena cava and/or abdominal aorta in 13 patients (transitional cell carcinoma three, nephroblastoma one, renal cell carcinoma nine). These were considered to be lymph node metastases. Angiography demonstrated malignant lymphatic spread in only two cases, with extensive neoplastic involvement of hilar and retroperitoneal lymphodes (Fig. 8). Enlarged lymph nodes were described in the operative reports in four cases, although in one of these histopathological examination of the resected node showed no evidence of tumour.

Distant metastatic spread

Distant metastases were found by CT in seven patients: bone three, liver three, lung one, viscera one. In only one case—with multiple peripancreatic and enteral metastases from a renal cell carcinoma (Fig. 9)—did angiography show the same as CT. Both methods were proved wrong by surgery in a case of hepatic haemangioma (Fig. 5).

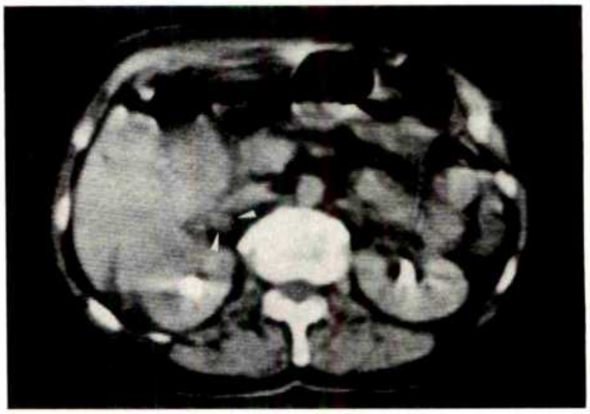


Fig. 7.
Lymph node involvement. CT: enlargement of paracaval lymph node.

TABLE V
Accuracy of angiography and CT in staging according to Robson's classification (1969)

Staging according to Robson	N	Angio	CT
I Intrarenal tumour	10	9/10	8/10
II Perirenal spread	12	9/12	11/12
III Vascular and/or lymph node involvement	8	6/8	7/8
IV Pararenal spread and/or distant metastasis	10	3/10	8/10
Total	40	27/40	34/40

In one case a second transitional cell carcinoma was discovered within the contralateral kidney, which had not been found by angiography.

Discussion

Accurate staging of renal malignant mass lesions is of great importance for both therapy planning and prognosis. In the staging system proposed by Robson *et al.* (1969), stage I tumours are confined within the renal capsule, whereas in stage II the malignancy is localized within the renal fascia of Gerota. Venous and/or lymphatic involvement is graded as stage III. Invasion of pararenal or intraperitoneal structures as well as distant metastases are grouped as stage IV. The extent of the tumour is important in planning surgery (Robson *et al.*, 1969; Skinner *et al.*, 1972) and may affect the decision to undertake transcatheter embolization, either preoperatively or palliatively

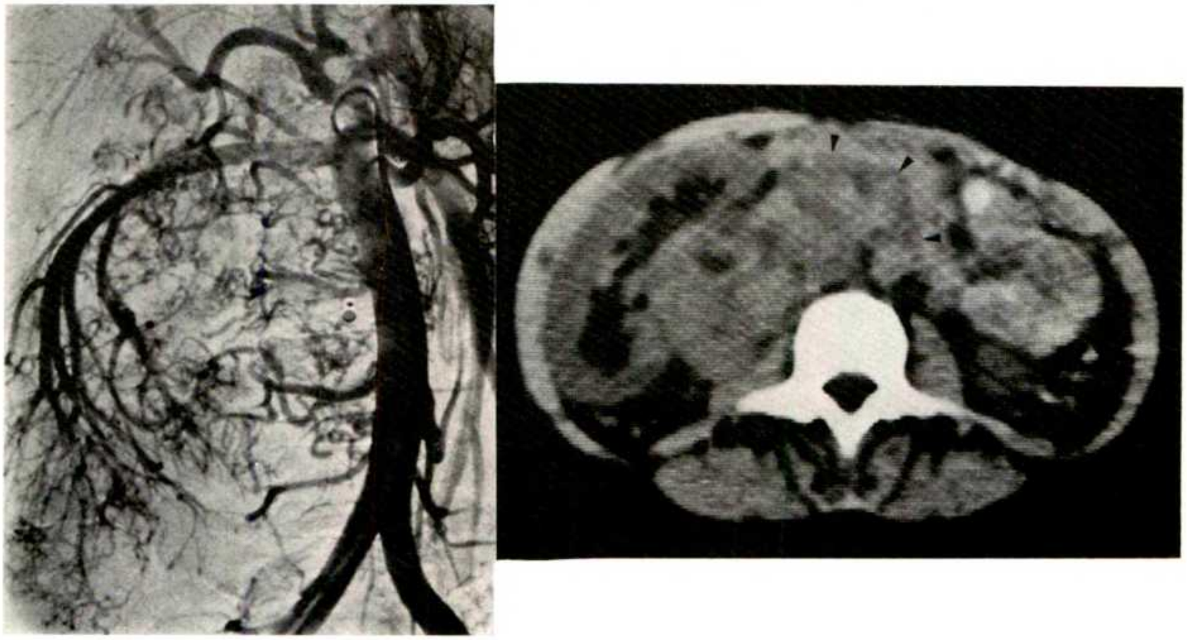


FIG. 8.

Lymph node involvement. (A) Angiography: clusters of malignant vessels next to the deviated aorta. (B) CT: extensive retroperitoneal nodular densities with partial obliteration of vena cava and aorta.

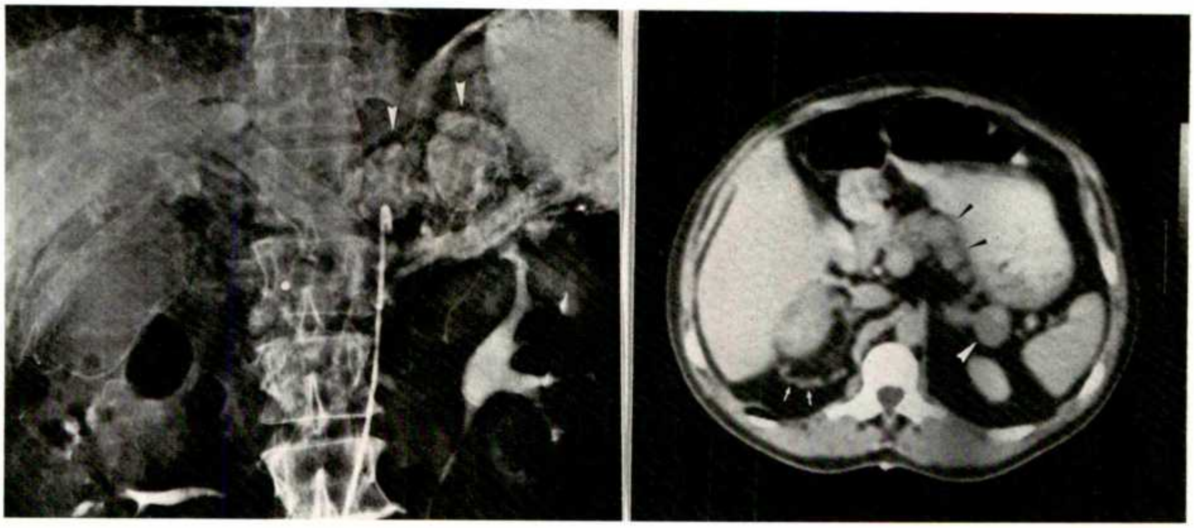


FIG. 9.

Distant metastases. (A) Angiography: large peripancreatic metastases of right sided hypernephroma. (B) CT: corresponding nodular densities in the splenic hilum and along splenic vessels. Note large perirenal collaterals due to occlusion of segmental renal vein. Main renal vein patent.

(Bücheler *et al.*, 1976; Goldstein *et al.*, 1976; Haertel and Kunz, 1975; Steckenmesser *et al.*, 1976; Thelen *et al.*, 1976). It also has prognostic value, for according to Robson *et al.* (1969), five-year survival decreased from 66% for stage I to 11% for stage IV.

Both angiography and CT can be difficult to interpret where the tumour has spread into the peri- or pararenal space (Table V). It is known that retroperitoneal or capsular collaterals may be demonstrated by angiography where the renal capsule is still intact

(Boijsen and Folin, 1961; Buist, 1974). Accordingly, saprophytic collateral supply from visceral arteries proves perirenal spread but does not necessarily indicate net tumour infiltration of visceral structures (Haertel and Kunz, 1975). Infiltration is, however, likely if the collaterals are obviously hypertrophied (Boijsen and Folin, 1961).

With CT, on the other hand, it is difficult to differentiate perirenal tissue reaction from small vascular structures or true infiltration (Baert *et al.*, 1979; Haertel and Kunz, 1975; Levine *et al.*, 1979), but pararenal tumour spread into the paravertebral musculature may be easily detected by the change of density. CT can easily demonstrate cranial tumour extension via the prevertebral retrocrural space into the mediastinum (Callen *et al.*, 1977). It is more difficult to differentiate spread towards or into a parenchymatous organ or gut, because the fat planes may be lacking. In our experience CT shows a higher diagnostic accuracy than angiography regarding peri- and pararenal tumour spread.

Twenty to fifty per cent of malignant renal tumours invade the renal vein (Goncharenko *et al.*, 1979; Robson *et al.*, 1969) and in approximately 5% of cases extend further into the inferior vena cava (Skinner *et al.*, 1972). The renal vein and the IVC are more often involved on the right than on the left (Goncharenko *et al.*, 1979; McCullough and Gittes, 1974). Although the prognosis is worse with renal vein involvement (Robson *et al.*, 1979; Thompson *et* al., 1975), nephrectomy may still be acceptable if the caval tumour is removed (McCullough and Gittes, 1974; Skinner *et al.*, 1972). It is therefore important to know whether there is venous tumour spread, and the limit of its cranial extension. Angiography identifies malignant intravascular extension with a high degree of accuracy; usually renal angiography demonstrates venous involvement by a striated vessel appearance of tumour extension in the area of the renal pedicle and/or the lack of venous opacification, together with the appearance of retroperitoneal collaterals (Ferris *et al.*, 1968); but similar findings may be produced by the tumour merely compressing the vein (Boijsen and Folin, 1961).

CT allows a positive diagnosis where the diameter of the vein and vena cava are grossly enlarged (Levine *et al.*, 1979; Marks *et al.*, 1978). An abrupt change of diameter through a sequence of sections, together with pronounced perirenal collaterals, suggests malignant involvement of the renal vein (Haertel *et al.*, 1981). Tumour invasion of the right renal vein may be more difficult to discern because this vein is more oblique (Levine *et al.*, 1979); but, in our experience, the resulting changes in shape and size of the vein help to detect the tumour. In order to demonstrate the patency of the IVC, or the existence of intra-luminal filling defect, in doubtful cases we inject the contrast medium slowly and steadily into the vein, while taking a series of sections starting where the IVC enters the atrium. Filling defects must be evident in adjacent sections, particularly at the level of the contralateral renal vein, in order to differentiate from an inflow phenomenon (Haertel *et al.*, 1981).

Since CT still appears to be less reliable than angiography in detecting venous tumour involvement an inferior cavogram must be carried out unless CT has unambiguously demonstrated either patency or involvement of the IVC.

With lymphatic involvement prognosis is poorer (Skinner *et al.*, 1972; Thompson *et al.*, 1975). Proven lymphatic involvement occurred in only 7.5% of our cases, as opposed to 22.7% of Robson's (1969). Malignant spread to the regional lymph nodes has not been systematically investigated surgically. The diagnostic accuracy of evaluation of malignant lymph node metastases could not, therefore, be assessed, and hence the numbers of the stage III cases in Table V must be regarded with caution. Enlarged lymph nodes were detected by CT in 30% of our cases, indicating more frequent presence of malignant involvement. Enlargement of lymph nodes may, however, be caused by non-specific benign reactive changes, leading to a false positive CT diagnosis of malignant involvement. Angiography demonstrates lymph node metastases of hypervascularized malignant renal tumours only when they have grown to a large size.

One of the major advantages of CT over any other renal diagnostic procedure is that it can demonstrate distant metastases and thus prove stage IV disease (Haertel *et al.*, 1981; Kreel, 1978; Stewart *et al.*, 1978) (Table V). Although our study has underestimated the sensitivity of angiography, particularly regarding liver metastases (for lack of routine coeliac investigation which Hellekant and Nyman (1979) found would show liver metastases in up to 17% of patients with renal malignancies), CT still gives much more information, especially as the bones and the lung bases are routinely examined. If a localized less dense liver process is present, or if the lesion is partly calcified, a late CT-scan of that region must be obtained after 10–15 minutes; if the lesion is further enhanced, haemangioma is more likely than a metastasis.

The diagnostic accuracy of angiography and CT for renal mass lesions is about the same. Hypovascular mass lesions consistently prove to be the major diagnostic challenge in differentiating between necrotic malignancies and inflammatory pseudotumours.

The greatest diagnostic problem in our experience is the CT evaluation of mass lesions with low attenuation values and insignificant enhancement, *i.e.* differentiation of complicated cysts, abscesses and partially necrotic malignancies. Extensive peritumoral transudation, sometimes extending into the abdominal wall, atonic bowel loops and the absence of enlarged lymph nodes may suggest an inflammatory lesion. In these ambiguous cases CT, or US guided aspiration for cytological diagnoses, must be performed (Stewart *et al.*, 1978; Triller, 1979; Vock, 1979).

Conclusion

The data we have presented confirm the conclusion reached by other authors (Baert *et al.*, 1979; Levine *et al.*, 1979; Love *et al.*, 1979), that CT is more accurate than angiography in the evaluation of perirenal and pararenal extension of malignant renal neoplasm (T-staging). CT is also better for detecting malignant lymphatic spread (N-staging) and distant metastases (M-staging). CT should be the preferred method for the investigation of patients with renal malignant mass lesions prior to treatment. It can be supplemented by angiography to aid in the evaluation of possible intravascular venous tumour invasion.

REFERENCES

Baert, A. L., Marchal, G. and Wilms, G., 1979. Les possibilités actuelles des scanners T.C. rapides dans le domaine rénal. *Journal de Radiologie, 60,* 723–732.

Boijsen, E. and Folin, J., 1961. Angiography in the diagnosis of renal carcinoma. *Radiologe, 1,* 173–191.

Bücheler, E., Hupe, W., Hertel, E. U. and Klosterhalfen, H., Katheterembolisation von Nierentumoren. *Fortschritte auf dem Gebiete der Röntgenstrahlungen, 124,* 134–138.

Buist, T., 1974. Parasitic arterial supply to intracapsular renal cell carcinoma. *American Journal of Roentgenology, 120,* 653–659.

Callen, P. W., Korobkin, M. and Isherwood, I., 1977. Computed tomographic evaluation of the retrocrural prevertebral space. *American Journal of Roentgenology, 129,* 907–910.

Ferris, E. J., Bosniak, M. A. and O'Connor, J. F., 1968. An angiographic sign demonstrating extension of renal carcinoma into the renal vein and vena cava. *American Journal of Roentgenology, 102,* 384–391.

Goldstein, H. M., Wallace, S., Anderson, H. J., Bree, R. L. and Gianturco, C., 1976. Transcatheter occlusion of abdominal tumours. *Radiology, 120,* 539–545.

Goncharenko, V., Gerlock, A. J., Kadir, S., Turner, B., 1979. Incidence and distribution of venous extension in 70 hypernephromas. *American Journal of Roentgenology, 133,* 263–265.

Haertel, M. and Kunz, R., 1975. Mesenteriale Vaskularisation maligner Nierentumoren. *Fortschritte auf dem Gebiete der Roentgenstrahlungen, 123,* 338–341.

Haertel, M., Probst, P., Zingg, E. and Fuchs, W. A., 1981. Renale Computertomographie. *Deutsche medizinische Wochenschrift, 106,* 54–59.

Hellekant, Ch., and Nyman, U., 1979. Routine celiac angiography in patients with renal cell carcinoma. *Journal of Urology, 122,* 17–19.

Kreel, L., 1978. Computed axial tomography in the diagnosis and treatment of malignancy. *Cancer Treatment Revue, 5,* 117–129.

Levine, E., Lee, K. R. and Weigel, J., 1979. Preoperative determination of abdominal extent of renal cell carcinoma by computed tomography. *Radiology, 132,* 395–398.

Love, L., Churchill, R., Reynes, C., Schuster, G. A., Moncada, R. and Berkow, A., 1979. Computed tomography staging of renal carcinoma. *Urological Radiology, 1,* 3–10.

Marks, W. M., Korobkin, M., Callen, P. W. and Kaiser, J. A., 1978. CT Diagnosis of tumor thrombosis of the renal vein and inferior vena cava. *American Journal of Roentgenology, 131,* 843–845.

McCullough, D. L. and Gittes, R. F., 1974. Vena cava resection for renal cell carcinoma. *Journal of Urology, 112,* 162–167.

Robson, Ch. J., Churchill, B. M. and Anderson, W., 1969. The results of radical nephrectomy for renal cell carcinoma. *Journal of Urology, 101,* 267–301.

Skinner, D. G., Pfister, R. F. and Colvin, R., 1972. Extension of renal carcinoma into the vena cava: The rationale for aggressive surgical management. *Journal of Urology, 107,* 711–716.

Steckenmesser, R., Bayindir, S., Rothauge, C. F., Nöske, K. and Weidner, W., 1976. Embolisation maligner Nierentumoren. *Fortschritte auf dem Gebiete der Röntgenstrahlungen, 125,* 251–257.

Stewart, B. H., James, R., Haaga, J. and Alfidi, R. J., 1978. Urological applications of computerized axial tomography: a preliminary report. *Journal of Urology, 120,* 198–204.

Thelen, M., Brühl, P., Gerlach, F. and Biersack, H. J., 1976. Katheterembolisation von metastasierten Nierenkarzinomen mit Butyl-2-Cyanoacrylat. *Fortschritte auf dem Gebiete der Röntgenstrahlungen, 124,* 232–235.

Thompson, I. M., Shannon, H., Ross, G. and Montie, J., 1975. An analysis of factors affecting survival in 150 patients with renal carcinoma. *Journal of Urology, 114,* 694–696.

Triller, J., 1979. Ultraschallgezielte abdominale Punktionen. *Radiologe, 19,* 173–181.

Vock, P., 1979. Computertomographisch gezielte Nadelpunktion. *Radiologe, 19,* 182–186.

1981, *British Journal of Radiology*, *54*, 754–757

Inversion of the right hemidiaphragm shown on ultrasound examination

By S. H. Lowe, M.A., F.R.C.R., D. O. Cosgrove, M.Sc., M.R.C.P. and A. E. A. Joseph, M.Sc., F.R.C.R.

Department of Radiology, St. George's Hospital, London SW17 and Department of Nuclear Medicine, Royal Marsden Hospital, Sutton, Surrey

(*Received February 1980 and in revised form April 1981*)

ABSTRACT

Inversion of the left hemidiaphragm has been reported previously but inversion of the right hemidiaphragm has been thought not to occur. Seven cases of inversion of the right hemidiaphragm demonstrated on routine ultrasound examination are reported, and the clinical implications are discussed.

Inversion of the left hemidiaphragm is visible on the plain chest film, being outlined by the air above the hemidiaphragm, or, when the hemithorax is opaque, by inference from the position of the air-filled gastric fundus. This subject has previously been discussed by Mulvey (1965) and Felson (1973); Swingle *et al.* (1969) recorded 11 cases occurring within one year. However, while depression of the right hemidiaphragm occurs, and, when the right hemithorax is opaque, can be inferred from descent of the right lobe of the liver on chest or abdominal X-ray, inversion, that is, reversal of the normal curvature of the hemidiaphragm, has been thought not to occur because of the splinting effect of the liver.

We present seven cases where inversion of the right hemidiaphragm was demonstrated on ultrasound examination.

PATIENTS AND METHODS

The examinations were performed on a custom-built grey-scale machine which has previously been discussed (Hill and Carpenter, 1975; Taylor and Hill, 1975; Taylor *et al.*, 1974). A 3 MHz transducer was used. One patient was also examined using an EMISONIC 4500 real time machine, and one patient was examined using a Diasonograph 4102 with grey-scale attachment.

The patients were undergoing routine examination of the liver, either before or during treatment of malignancy. All had large right pleural effusions.

CASE REPORTS

Case 1

A 42-year-old male developed pleural metastases one year after a right orchidectomy for an intermediate teratoma. He then developed a right pleural effusion which was aspirated. Ultrasound examination following this was normal. The effusion recurred and a chest X ray showed an opaque hemithorax. Ultrasound examination then showed gross downward displacement of a normal liver with complete inversion of the right hemidiaphragm (Fig. 1). Pleural and mediastinal deposits were identified which had previously been demonstrated on chest X ray. A further ultrasound examination two weeks later following partial aspiration of the effusion showed the diaphragmatic inversion, though still present, to be less marked (Fig. 2). No hepatic metastases were seen at post mortem; there was a 4 l right pleural effusion.

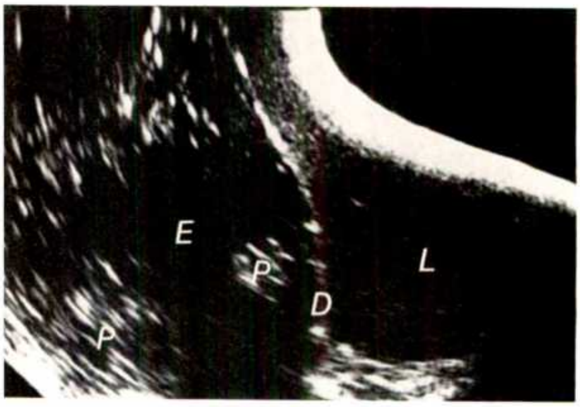


FIG. 1. *Case 1.*

The diaphragm is depressed and inverted. Echogenic masses seen within the effusion could be correlated with pleural metastases seen on chest X ray when the pleural effusion was smaller. D—Diaphragm, E—Effusion, L—Liver, P—Pleural metastases. (The same notation is used in all Figures.)

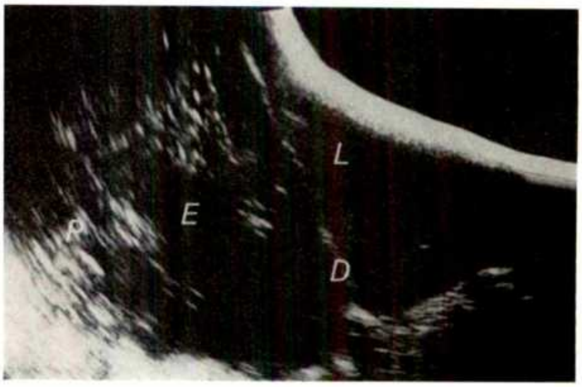


FIG. 2. *Case 1.*

Following aspiration, a scan in the same position as Fig. 5 shows the diaphragm less inverted.

Case 2

A 65-year-old male with carcinoma of the right main bronchus presented with dyspnoea, and was found clinically and radiologically to have a massive right pleural effusion. The liver was shown to be normal on ultrasound examination but depressed by a large right pleural effusion (Fig. 3). A mass noted within the chest on this examination was shown at post mortem one month later to be right lung infiltrated by tumour. No metastases were seen in the liver.

Case 3

A 78-year-old female with carcinoma of the breast diagnosed twelve years previously presented with dyspnoea and a large right pleural effusion. Physical examination demonstrated the lower border of the liver at the level of the umbilicus. Ultrasound showed a normal liver displaced downwards by a large pleural effusion (Fig. 4). The right hemidiaphragm was inverted and the upper border of the liver lay below the costal margin. A further examination after treatment showed the hemidiaphragm in its normal position, though the effusion was still present (Fig. 5).

Case 4

A 65-year-old male presented with a right pleural effusion which yielded poorly differentiated squamous cells and which did not respond to treatment. Ultrasound examination showed a normal liver displaced downward and medially by a large pleural effusion. The right hemidiaphragm was inverted.

Case 5

A 31-year-old woman with well-differentiated mesothelioma had a recurrence of her right pleural effusion six years after initial diagnosis and pleurectomy. Ultrasound examination showed a normal liver displaced downwards to the level of the umbilicus by a massive right pleural effusion. The right hemidiaphragm was inverted. Paradoxical movement of the right hemidiaphragm during quiet breathing was observed using real time ultrasound.

Case 6

A 65-year-old female presented with a large right pleural effusion and over the next six months developed right hilar and right paratracheal masses. Histological examination could not suggest a primary site. Ultrasound examination showed a normal liver displaced downwards and to the left by a large right pleural effusion. There was a soft tissue mass adjacent to the right hemidiaphragm which was inverted except where it was in contact with the mass (Fig. 6 and 7).

Case 7

A 74-year-old male presented with recent dyspnoea and pain in the back and right chest. Chest X ray showed an opaque right hemithorax with some mediastinal shift to the left. Diagnostic pleural aspiration produced blood-stained fluid containing cells suggestive of malignancy. Ultrasound examination after aspiration of one litre of fluid showed gross downward displacement of the right hemidiaphragm and shift of the liver and major abdominal vessels to the left

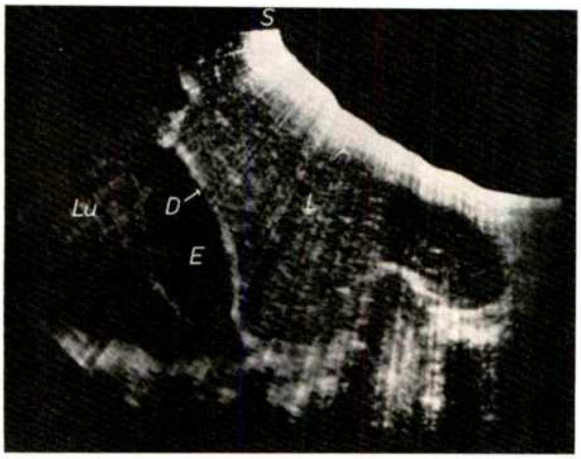


FIG. 3. *Case 2.*

The diaphragm is inverted. An echogenic mass seen within the effusion proved to be tumour infiltrating lung tissue at post mortem. Lu—Lung.

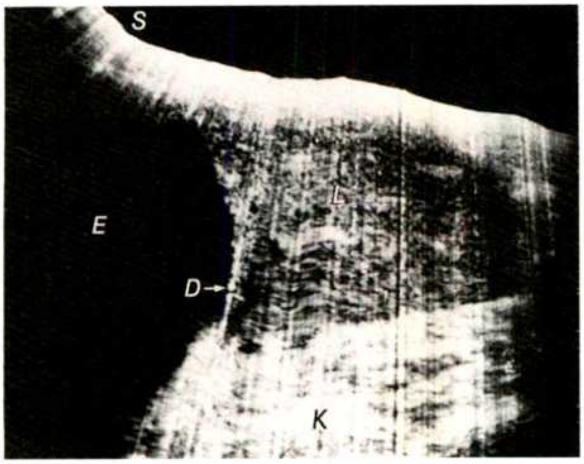


FIG. 4. *Case 3.*

The diaphragm is depressed by a large pleural effusion. K—Kidney.

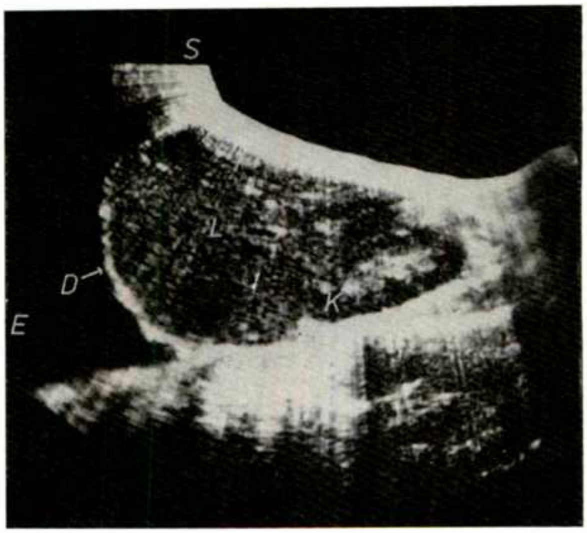


FIG. 5. *Case 3.*

Though the effusion is still present its volume is smaller, and the diaphragm is shown in the normal position. The position of the scan is equivalent to Fig. 4. K—Kidney, S—Skin.

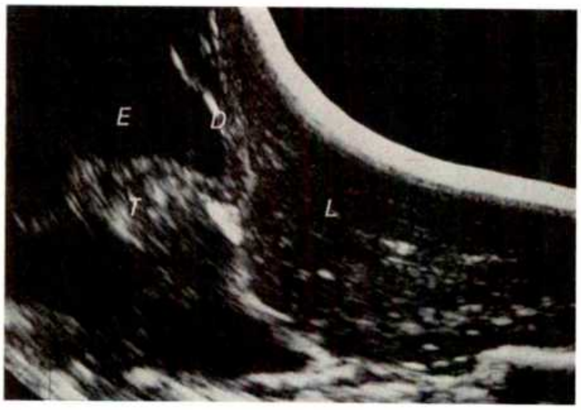


FIG. 6. *Case 6.*
The diaphragm is inverted except where in contact with a large mass. T—Tumour.

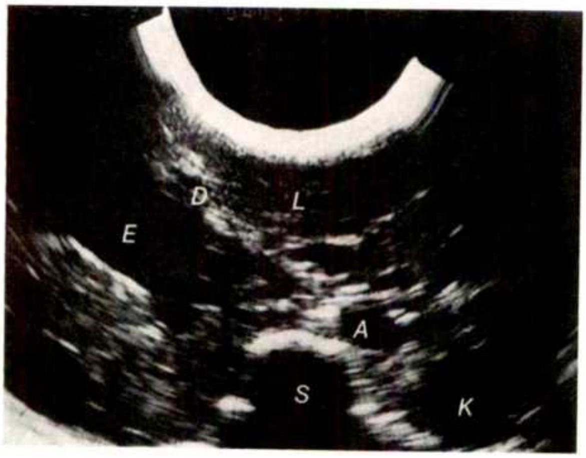


FIG. 7. *Case 6.*
Transverse section across the upper abdomen. The right lobe of the liver is depressed below the plane of this section. A—Aorta, K—Kidney, L—Left lobe of liver, S—Spine.

(Fig. 8). After aspiration of a further litre of fluid, the right hemidiaphragm moved toward a more normal position (Fig. 9) though the chest X ray was unchanged. Further examinations were not possible.

DISCUSSION

Mulvey (1965) presented a number of cases where massive pleural effusions on the left had caused inversion of the hemidiaphragm. He observed paradoxical movement of the left hemidiaphragm as indicated by the position of the gastric air bubble, on screening during quiet respiration, and discussed the effect this may have on respiratory function. Moreover, he suggested that the clinical benefit gained by thoracocentesis might be small if this only rendered the inverted hemidiaphragm apparently paretic, and the patient's condition might even be worsened. Apparent paresis of the hemidiaphragm occurs when it is flattened such that contraction of its muscular part can cause no movement. He stated that he had not seen even indirect evidence for inversion of the right hemidiaphragm (paradoxical excursion of the upper level of a right pleural effusion during quiet respiration).

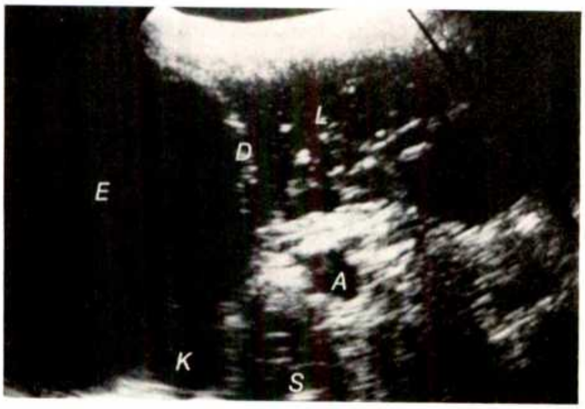


FIG. 8. *Case 7.*
Transverse section 2 cm below xiphisternum. Note the displacement of the liver and major vessels. The medial margin of the right hemidiaphragm is visualized. A—Aorta, K—Right Kidney, S—Spine.

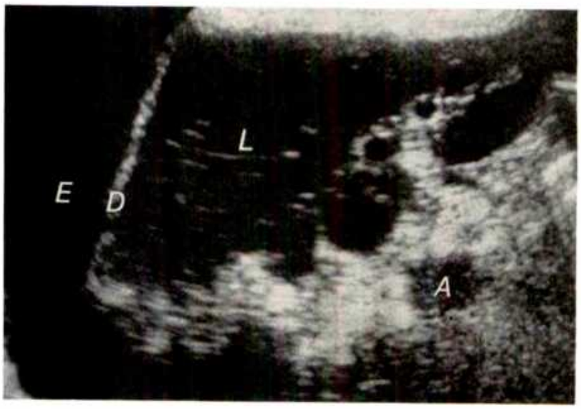


FIG. 9. *Case 7.*
Transverse section. The liver and major vessels are now in a more normal position. Compare with Fig. 8. A—Aorta.

Felson (1973) described two infants with inversion of the right hemidiaphragm due to tension pneumothorax and to congenital emphysema. He speculated that the liver must ordinarily prevent the inversion of the right hemidiaphragm due to pleural fluid or an intrathoracic mass. However, Kawata *et al.* (1977) suspected inversion of the right hemidiaphragm on liver scintigraphy in a woman with bilateral breast carcinomas. This was confirmed on chest X ray by instilling water-soluble contrast medium into the pleural space after the removal of some fluid.

Cunningham (1978), in a discussion of grey scale echography of the lung and pleural space, demonstrated, among other examples of pleural effusion, a scan of the chest of a woman with carcinoma of the breast in whom the hemidiaphragm was inverted in the presence of a massive right pleural effusion, and Katzen *et al.* (1978) illustrated in a case report the time consuming diagnostic problem that can be caused if this possibility is not appreciated.

We present here a further seven cases of inversion of the right hemidiaphragm due mainly to the presence of massive pleural effusions, though in some patients a soft tissue mass also contributed. Inversion of the right hemidiaphragm is thus possible, and may be quite common in the presence of a large effusion. It should certainly be considered in cases of large pleural effusion due to malignancy where clinical hepatomegaly suggests hepatic metastases, and also in those cases where clinical improvement in dyspnoea fails to occur following aspiration of an effusion; and it can be detected simply and rapidly by routine ultrasound examination.

ACKNOWLEDGMENTS

Thanks are due to Mrs. S. Gillingham and Miss J. Olejnik for secretarial assistance and to T. Suzuki for help in translation.

REFERENCES

CUNNINGHAM, J. J., 1978. Grey scale echography of the lung and pleural space. *Cancer, 41,* 1329–1339.

FELSON, B., 1973. *Chest Roentgenology.* (W. B. Saunders, Philadelphia), p. 428.

HILL, C. R. and CARPENTER, D. A., 1975. Ultrasonic echo imaging of tissues: instrumentation. *British Journal of Radiology, 49,* 238–43.

KATZEN, B. T., CHOI, W. S., FRIEDMAN, M. H., GREEN, I. J., HINDLE, W. V. and ZELLIS, A., 1978. Pseudomass of the liver due to pleural effusion and inversion of the diaphragm. *American Journal of Roentgenology, 131,* 1077–1078.

KAWATA, Y., KUBOTA, T. and NAKAMURA, M., 1977. Inversion of the (R) hemidiaphragm due to pleural fluid. *Japan Journal Clinical Radiology, 22,* 149–153.

MULVEY, R. B., 1965. The effect of pleural fluid on the diaphragm. *American Journal of Roentgenology, 84,* 1080–1085.

SWINGLE, J. A., LOGAN, R. and JUHL, J. H., 1969. Inversion of the left hemidiaphragm. *Journal of the American Medical Association, 208,* 863–864.

TAYLOR, K. J., CARPENTER, D. A. and MCREADY, V. R. 1974. Ultrasound and scintigraphy: the differential diagnosis of obstructive jaundice. *Journal of Clinical Ultrasound, 2,* 105–116.

TAYLOR, K. J. and HILL, C. K., 1975. Scanning techniques in grey scale ultrasonography. *British Journal of Radiology, 48,* 918–20.

Book review

Abdominal Ultrasound in the Cancer Patient. By D. J. Brascho and T. H. Shawker, pp. xv+414, 1980 (John Wiley & Sons, Chichester/New York), £21·00.
ISBN 0–471017426

The authors feel that ultrasound is undervalued as an investigative technique for abdomino-pelvic disease in the diagnosis and management of tumours. Implicit in this assumption is the contention that other imaging methods have acquired an over-inflated value, abdominal CT scanning being the major competitor. To a large extent they have made their point, aided by able colleagues specialising in ultrasound in paediatrics (Drs. B. M. Potter and J. L. Frank) and in the digestive tract (Drs. E. I. Bluth and C. R. B. Merritt). The one exception seems to be the exaggerated claims for the usefulness of ultrasound in radiotherapy planning where the difficulties of supplying all of the relevant information are underplayed; most radiotherapists are in no doubt that CT is a more reliable technique here, albeit with some important exceptions. This section apart, the excellent text presents a balanced view of the applications of ultrasound throughout the abdomen with useful clinical background into which sonography is integrated. Sadly the images are substandard and, though well labelled and annotated, do not do justice to the text or the authors' intention to "present a text that is clinically orientated but well illustrated". Sometimes the value of alternative imaging techniques, both traditional and new, has been underrated, an example being the surprising statement that lymphography is no longer usually required for the staging and management of testicular teratoma since it is "useful only in the presence of gross deposits in the lymph nodes". Not everyone would agree either with the contention that it is the degree of acoustic impedance mismatch that leads to specular reflections in an otherwise useful and apposite discussion of the relationship between the ultrasound image and the tissue structure that gives rise to it. (In fact specular echoes arise when the interface is smooth or flat over a distance of several wavelengths, as is correctly stated elsewhere in the same discussion.)

The section on paediatric applications must be singled out as outstanding in its clarity, comprehensiveness and clinically orientated evaluation of the relative uses of various imaging techniques in childhood tumours.

Overall this is an excellent text, somewhat let down by its illustrations, that should be read and re-read by all those involved in imaging in oncology. It should also be available for reference by clinical oncologists.

DAVID O. COSGROVE.

1981, *British Journal of Radiology*, 54, 758–761

Atlanto-occipital and atlanto-axial dislocations with spinal cord compression in Down's syndrome: a case report and review of the literature

By *G. D. Hungerford, M.B., B.S., D.D.R., M.R.A.C.R., *V. Akkaraju, M.D., †S. E. Rawe, M.D., F.A.C.S. and ‡G. F. Young, M.D.

Departments of *Radiology, †Neurosurgery and ‡Neurology, Medical University of South Carolina, 171 Ashley Avenue, Charleston, SC 29403, USA

(*Received February, 1981*)

ABSTRACT

A case of Down's syndrome who has survived dislocation of both the atlanto-occipital and atlanto-axial joints is described and reviewed together with 11 cases culled from the literature.

Death can result from atlanto-axial dislocation, but many patients with this condition do survive and may be seen with reasonable frequency at any large teaching hospital. Disruption of the atlanto-occipital joint is very rarely seen, however, and few survivors of atlanto-occipital dislocation have been reported. In this report, we describe a girl who has survived dislocation of both the atlanto-occipital and atlanto-axial joints. She is of further interest because she represents the first case of atlanto-occipital subluxation associated with Down's syndrome, and is also a rare example of Down's syndrome with spinal cord compression.

CASE REPORT

The patient is a 15-year-old girl with known Down's syndrome who had been the product of an uncomplicated pregnancy and normal vaginal delivery of a 33-year-old mother. She presented at the age of 14 years with a history of increasing difficulty in walking for four months, decreasing use of her left hand for three months, and right-sided headaches. Physical examination showed an alert, but mentally retarded, child with a quadriparesis in which the left side was worse than the right. She was still able to walk with a stiff-legged broad-based gait. There were no sensory deficits. Deep tendon reflexes were increased bilaterally and the plantar reflexes were upgoing on both sides. Plain radiographs of the cervical spine (Fig. 1) showed instability of the cranio-cervical region with subluxation and instability at both the atlanto-occipital and atlanto-axial levels. In mid-position the gap between the odontoid process and the anterior arch of the atlas was 11 mm, and there was a small bone fragment above the anterior arch of the atlas, probably representing an ossiculum terminale (Greenberg, 1968). Myelography was attempted with a lumbar injection of metrizamide (Fig. 2). This was only partially successful, as it was considered unsafe to extend the patient's head far enough to pool the metrizamide in the craniocervical region. Nevertheless, it showed a partial block at the C1 level and marked narrowing of the subarachnoid space. Immediately following the myelogram the patient was transferred to the computed tomography (CT) scanner where a series of axial cuts through the cranio-cervical region was obtained (Fig. 3). These clearly showed severe cord compression behind the odontoid process (where the sagittal diameter of the cord was reduced to approximately 1.5 mm), and tissue filling the space between the odontoid process and the anterior arch of the atlas. Reformatting of this information in the sagittal and coronal planes demonstrated these findings from a different perspective. Approximately six months after the onset of her symptoms she underwent surgery with posterior fusion of the occiput to C1, C2, and C3 using iliac bone. In the initial post-operative period her neurological function deteriorated, but it subsequently returned to the pre-operative level.

Six months after surgery, her neurological function had not significantly improved. A repeat CT metrizamide study

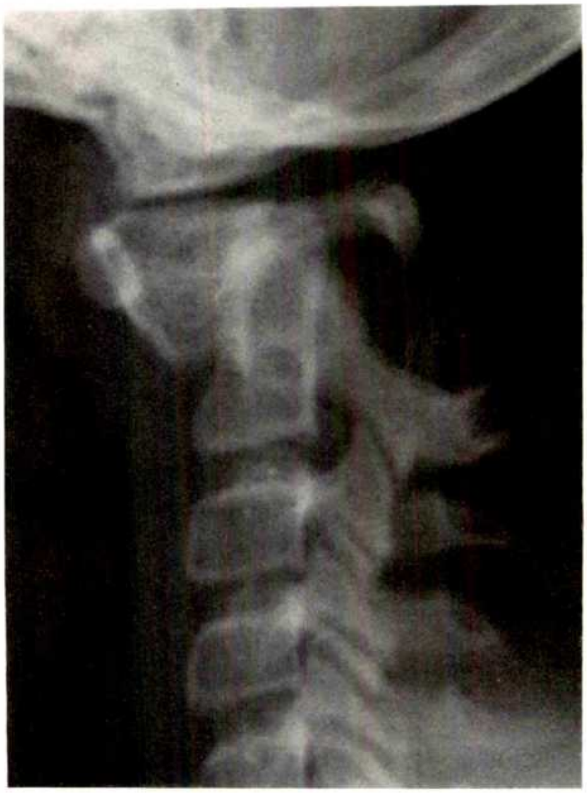


FIG. 1A.

Lateral view of the cervical spine in flexion. There is marked subluxation of the atlas on the axis, but the occiput and atlas are in a normal relationship.

showed essentially unchanged findings with severe compression of the cervical cord behind the odontoid process. Although flexion and extension films revealed no instability of the atlanto-occipital and atlanto-axial joints, the space between the odontoid process and the posterior arch of the atlas was greatly reduced due to the fixed atlanto-axial dislocation. She has subsequently undergone transoral odontoidectomy, and is demonstrating clinical improvement.

DISCUSSION

Tishler and Martel (1965) first described atlanto-axial dislocation in a patient with Down's syndrome, and since then it has become clear that this association is common, occurring in 14 of 70 children in one series (Martel and Tishler, 1966). Semine *et al.* (1978) found abnormalities of the C1-C2 articulation in 18% of 85 children with Down's syndrome. Twelve per cent had subluxation alone and 6% had associated abnormalities of the odontoid process. The cause of the atlanto-axial subluxation in Down's syndrome is still debated. Tishler and Martell (1965) first suggested that it was due to laxity of the transverse ligament, possibly as part of a generalized increase in ligamentous laxity which has been observed in Down's syndrome (Semine *et al.*, 1978). Abnormal development of the odontoid process may also predispose to atlanto-axial subluxation and an increased incidence of such abnormalities has been noted in Down's syndrome (Semine *et al.*, 1978) including odontoid dysplasia, hypoplastic odontoid, os odontoideum, ossiculum terminale, and a "third condyle" or manifestation of an occipital vertebra.

Atlanto-occipital dislocation is rarely seen in living patients. Only nine cases due to trauma have been described (Powers *et al.*, 1979), of whom six survived. Atlanto-occipital dislocation due to causes other than trauma appears to be extraordinarily rare and in a limited review of the literature we found two cases associated with rheumatoid arthritis (Martel, 1961; Bunton *et al.*, 1978) and one caused

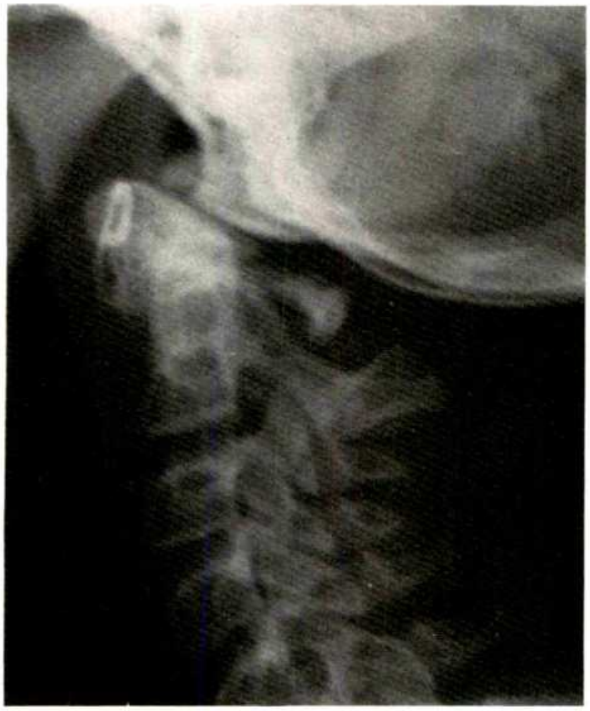


FIG. 1B.

Lateral view of cervical spine in extension. The occiput has now slipped posteriorly in relation to the atlas. The atlanto-axial subluxation is less marked.

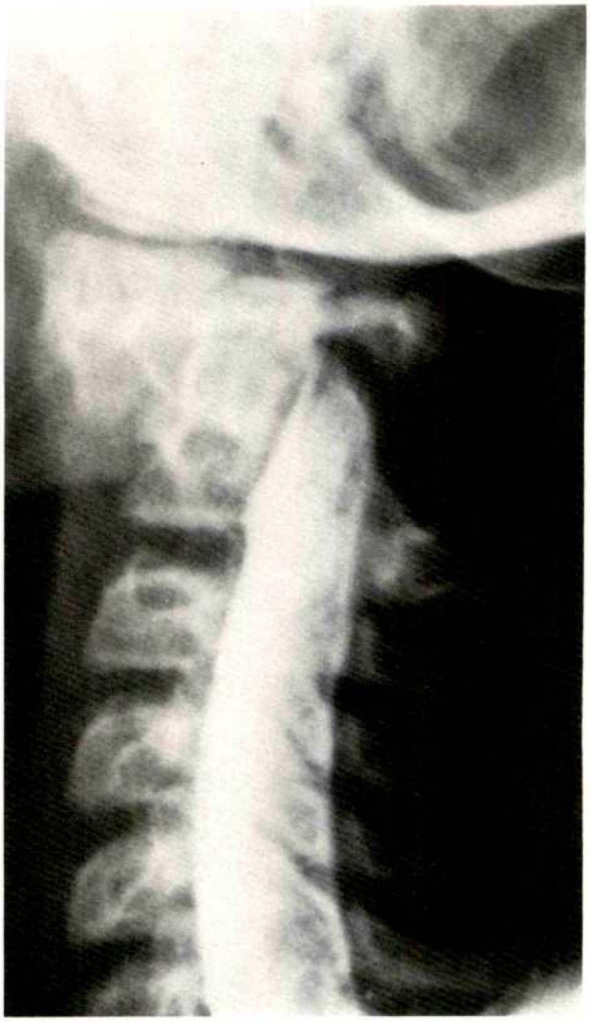


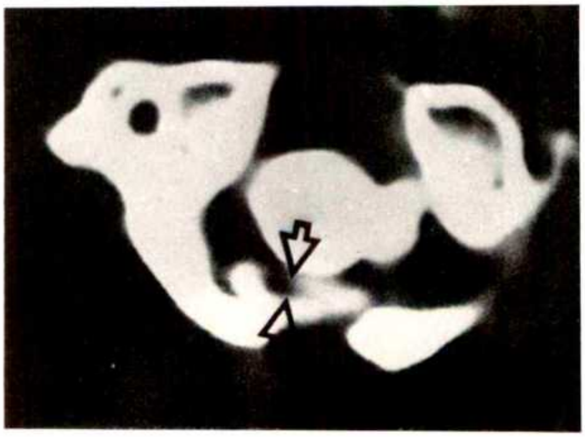
FIG. 2.

Metrizamide myelogram showing marked narrowing of the subarachnoid space behind the odontoid process.

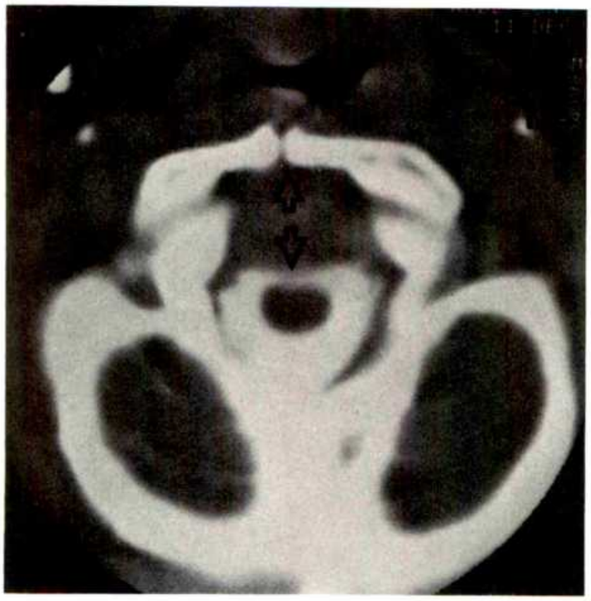
by a pituitary adenoma which eroded the clivus (Laws and Ivins, 1979). The aetiology of the atlanto-occipital dislocation in our case is uncertain, but presumably the same mechanism was responsible for the dislocations of both the atlanto-occipital and atlanto-axial joints as there was no history of trauma or any other antecedent cause. Atlanto-occipital dislocation has not previously been described in Down's syndrome.

Despite the increased frequency of cervical abnormalities, spinal cord compression and neurological deficit have been described in only 11 previous cases of Down's syndrome (Table I). In some of these the dislocation has been irreducible and at autopsy in one girl (Sherk and Nicholson, 1969) the transverse ligament had slipped under an ossiculum terminale, suggesting that this mechanism operates to prevent reduction in some patients. The CT findings in our case, however, suggest that tissue deposition in the space between the atlas and odontoid also plays a part in preventing reduction. The outcome, once neurological deficit has occurred, is variable (Table I) but decompression and fusion have been helpful in seven of the 12 patients. Giblin and Micheli (1979) reviewed the management of seven cases and recommended initial stabilization and posterior fusion, possibly followed by odontoidectomy if necessary. They caution that posterior decompression alone, with excision of the posterior arch of C1, may result in instability of the cranio-cervical region leading to further clinical deterioration.

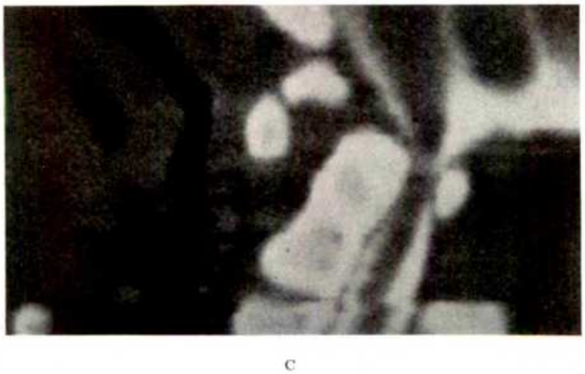
Computed tomography, particularly when it is combined with subarachnoid metrizamide, often allows us to see spinal cord displacements and abnormalities much more clearly than is possible with myelography or any other diagnostic modality. In the present case, it is remarkable that spinal cord function was preserved to a moderate degree when the sagittal diameter of the cord had been reduced to only 1.5 mm as shown by the CT metrizamide study. This, however, is not unique in our experience and we have seen several similar cases, some with only minimal neurological deficit.



A



B



C

FIG. 3.

(A) Axial CT metrizamide study showing severe compression of the spinal cord (arrows) behind the odontoid process.

(B) Axial CT metrizamide study at the level of the atlas showing tissue (arrows) filling the space between the anterior arch of the atlas and the subarachnoid space.

(C) Sagittal reformatting of the axial CT cuts showing compression of the cord behind the odontoid process.

TABLE I

DOWN'S SYNDROME WITH SPINAL CORD COMPRESSION

Author	Radiological findings	Clinical findings	Management	Result
Dzenitis, 1966	C1-C2 dislocation	Quadriparesis Neurogenic bladder	Reducation and posterior fusion	Almost complete recovery
Curtis *et al.*, 1969	C1-C2 dislocation	Slight weakness R. foot Increased reflexes R. leg	Partial reduction and posterior fusion	Full recovery
Martel *et al.*, 1969	C1-C2 dislocation "Third condyle"	Progressive quadriparesis for two years	Partial reduction and posterior fusion	Partial recovery
Sherk and Nicholson, 1968	C1-C2 dislocation ossiculum terminale	Quadriparesis for three years	No specific therapy	Died
Aung, 1973	C1-C2 dislocation, cord and medulla compressed	Quadriparesis L > R for two months	Decompression with neck brace	No improvement
Finerman *et al.*, 1976	C1-C2 dislocation, hypoplastic odontoid, ossiculum terminale	L hemiparesis and pain for five months	Decompression and posterior fusion	Complete recovery
Semine *et al.*, 1978	C1-C2 dislocation	Hyperreflexia and clonus	?	?
Giblin and Micheli, 1979	C1-C2 dislocation, platybasia, cord compression	Paraparesis for two years, sensory deficits	Decompression, posterior fusion odontoidectomy	No improvement
Giblin and Micheli, 1979	C1-C2 dislocation	Quadriparesis for 4 months Sensory deficits	Partial reduction and posterior fusion	Partial recovery
Dawson and Smith, 1979	C1-C2 dislocation, severe cervical cord compression	Paraesthesiae for 1½ years L hemiplegia	Decompression and posterior fusion	Symptom free
Dawson and Smith, 1979	C1-C2 dislocation	Hyperreflexia and clonus	Posterior fusion	Improved
Hungerford *et al.*, 1981	Atlanto-occipital & C1-C2 dislocation, ossiculum terminale, severe cord compression	Quadriparesis 4 months	Posterior fusion, odontoidectomy	Improved

REFERENCES

AUNG, M. H., 1973. Atlanto-axial dislocation in Down's syndrome. *Bulletin of the Los Angeles Neurological Society*, *38*, 197–201.

BUNTON, R. W., GRENNAN, D. M., PALMER, D. G., and DE SILVA, R. T. D., 1978. Lateral subluxation of the atlas in rheumatoid arthritis. *British Journal of Radiology*, *51*, 963–967.

CURTIS, B. H., BLANK, S., and FISHER, R. L., 1968. Atlanto-axial dislocation in Down's syndrome. Report of two patients requiring surgical correction. *Journal of the American Medical Association*, *205*, 464–213.

DAWSON, E. G. and SMITH, L., 1979. Atlanto-axial subluxation in children due to vertebral anomalies. *Journal of Bone and Joint Surgery*, *61-A*, 582–587.

DZENITIS, A. J., 1966. Spontaneous atlanto-axial dislocation in a mongoloid child with spinal cord compression. *Journal of Neurosurgery*, *25*, 458–460.

FINERMAN, G. A. M., SAKAI, D., and WEINGARTEN, S., 1976. Atlanto-axial dislocation with spinal cord compression in a mongoloid child. *Journal of Bone and Joint Surgery*, *58-A*, 408–409.

GIBLIN, P. E. and MITCHELL, L. J., 1979. The management of atlanto-axial subluxation with neurologic involvement in Down's syndrome: a report of two cases and review of the literature. *Clinical Orthopedics and Related Research*, *140*, 66–71.

GREENBERG, A. D., 1968. Atlanto-axial dislocations. *Brain*, *91*, 655–684.

LAWS, E. R. and IVINS, J. C., 1979. Atlanto-occipital instability as a result of pituitary adenoma: Case report with successful management by cervico-occipital fusion. *Johns Hopkins Medical Journal*, *145*, 136–138.

MARTEL, W., 1961. The occipito-atlanto-axial joints in rheumatoid arthritis and ankylosing spondylitis. *American Journal of Roentgenology*, *86*, 223–240.

MARTEL, W. and TISHLER, J. M., 1966. Observations on the spine in mongoloidism. *American Journal of Roentgenology*, *97*, 630–638.

MARTEL, W., UYHAM, R., and STIMSON, C. W., 1969. Subluxation of the atlas causing spinal cord compression in a case of Down's syndrome with a "manifestation of an occipital vertebra". *Radiology*, *93*, 839–840.

POWERS, B., MILLER, M. D., KRAMER, R. S., MARTINEZ, S., and GEHWEILER, J. A., 1979. Traumatic anterior atlanto-occipital dislocation. *Neurosurgery*, *4*, 12–17.

SEMINE, A. A., ERTEL, A. N., GOLDBERG, M. J. and BULL, M. J., 1978. Cervical spine instability in children with Down's syndrome (trisomy 21). *Journal of Bone and Joint Surgery*, *60-A*, 649–652.

SHERK, H. D., NICHOLSON, J. T., 1969. Rotatory atlanto-axial dislocation associated with ossiculum terminale and mongolism. A case report. *Journal of Bone and Joint Surgery*, *51-A*, 957–964.

TISHLER, J. and MARTEL, W., 1965. Dislocation of the atlas in mongolism. *Radiology*, *84*, 904–906.

1981, *British Journal of Radiology*, 54, 762–767

Isotope bone imaging in suspected scaphoid trauma

By *E. B. Rolfe, B.Sc., D.M.R.D., F.R.C.R, N. W. Garvie, M.A., M.Sc., D.M.R.D., F.R.C.R., M.R.C.P., M. A. Khan, M.B., B.S. and D. M. Ackery, M.A. M.Sc.

The Wessex Regional Deparment of Nuclear Medicine and the Accident and Emergency Department, Southampton General Hospital

(Received April 1980 and in revised form April 1981)

Abstract

The unreliability of radiological examination in excluding or confirming a suspected scaphoid fracture after carpal trauma is a well-recognised diagnostic problem. This paper explores the role of isotope bone imaging (IBI) in the early identification of carpal bone injury. Abnormal generalized uptake of activity may be seen within the carpus, possibly as a consequence of diffuse soft tissue injury, particularly if imaging is performed within 48 hours of trauma. A focal area of increased uptake related to one carpal bone is suggestive of fracture though the part which ligamentous injury, localized periosteal reaction or incomplete cortical infarction may play in the production of such radionuclide appearances is uncertain.

Ninety-nine patients with suspected recent scaphoid fracture but no demonstrable abnormality on radiological examination were subjected to IBI, using 555 MBq (15 mCi) of ^{99}Tc^{m} methylene diphosphonate. Abnormal focal increased uptake (AFIU) was found in 47 patients, this being localized to the scaphoid bone in 26. Of these 47 cases, 19 (42%) showed subsequent radiological evidence of facture.

The results of IBI, in our experience, can only be reliably interpreted if imaging is performed at least 48 hours after injury, though in cases of fracture AFIU may persist for several years. Using this technique, the possibility of fracture can be confidently excluded in that group of patients who show no AFIU. In selected cases of carpal trauma, IBI provides a satisfactory alternative means of identifying the presence and site of localized injury within the carpus and may be used to confidently exclude those patients with non-osseous symptomatology.

The advent of short-lived bone-seeking radio pharmaceuticals, together with advances in instrumentation in nuclear medicine, has significantly extended the general application of isotope bone imaging (IBI). IBI has been in the past principally applied to the detection of osseous metastases, and in this field has become well established (Sharma and Quinn, 1972; Pendergrass *et al.*, 1973). The role of IBI in traumatic bone disease is, however, much less clearly defined.

It is a recognized feature that in IBI bone-seeking radiopharmaceuticals will become selectively taken up and concentrated at sites of fracture, producing a characteristic "hot spot". This phenomenon arises from the avidity of such agents for areas of increased osteoblastic activity or hyperaemia and is observed in bone trauma of varying severity (James *et al.*, 1976; Tothill and McCormick, 1975). AFIU, as well as occurring in fracture, is, however, shown within a region of periosteal reaction secondary to a traumatic sub-periosteal haemorrhage (Rosenthall and Lisbona, 1980), and also possibly within ligamentous injury. In the absence of confirmatory radiographic evidence of fracture, no reliable means of the *in vivo* identification of the exact cause of abnormal focal increased uptake (AFIU) exists.

The present study has been undertaken to define the frequency and distribution of AFIU and therefore possible fracture within the carpus, in a group of patients with a diagnosis of suspected scaphoid fracture and normal initial radiographic examination. All patients who were investigated were referred through the Accident and Emergency Department.

Patients and Methods

Ninety-nine patients underwent IBI. The grounds for referral were: (1) Recent history of carpal trauma, (2) Clinical signs suggestive of a scaphoid fracture, (3) No identifiable fracture on initial radiographic examination.

IBI of the carpus was performed two hours after the intravenous injection of 555 MBq (15 mCi) of 99Tc^{m} methylene diphosphonate, using a Toshiba large field gamma camera. A total of 200 kilo counts was accumulated for each view, over a period of approximately 10 min, using a low-energy high-

TABLE I

Distribution of sites of AFIU in patients suspected of scaphoid fracture

Bone involved	Frequency affected	Percentage frequency
Scaphoid	26	52
Triquetrum	4	8
Distal radius	9	18
Capitate	2	4
Trapezoid	5	10
Hamate	1	2
1st metacarpal	2	4
2nd metacarpal	1	2
	Total 50	

Total number of patients 99.
Total with evidence of AFIU—47 (three patients had fractures at two sites).
Number of patients having AFIU with subsequent radiological evidence of fracture—19 (42%).

---

*Present address: Department of Diagnostic Radiology, The Queen Elizabeth Hospital, Edgbaston, Birmingham.

resolution parallel-hole collimator. The images were interpreted and correlated with the appropriate radiographs. AFIU was taken to indicate localized trauma provided that degenerative disease, a potential cause of a false positive examination, was excluded on radiographic examination.

RESULTS

These are presented in Table I. Of the 99 cases of suspected scaphoid trauma, 47 had AFIU. Three patients had AFIU at more than one site. Of the 47 patients with AFIU, only 26 had evidence of scaphoid injury. Of the positive group, 19 (42%) had retrospective radiographic evidence of a fracture, or showed such changes at a later date.

The time of imaging after trauma varied from two to 60 days with a mean of ten days, apart from one case unsuccessfully imaged at 12 hours. The average age of the patients was 23 years.

Examples

Figure 1 is the radiograph of a male (23 years) obtained four days after trauma. No fracture is visible. The radioisotope image (Fig. 2) taken 1 day later shows evidence of AFIU affecting the scaphoid. The fracture of the proximal pole of the scaphoid has been clearly visible on further X-ray examination three months later (Fig. 3).

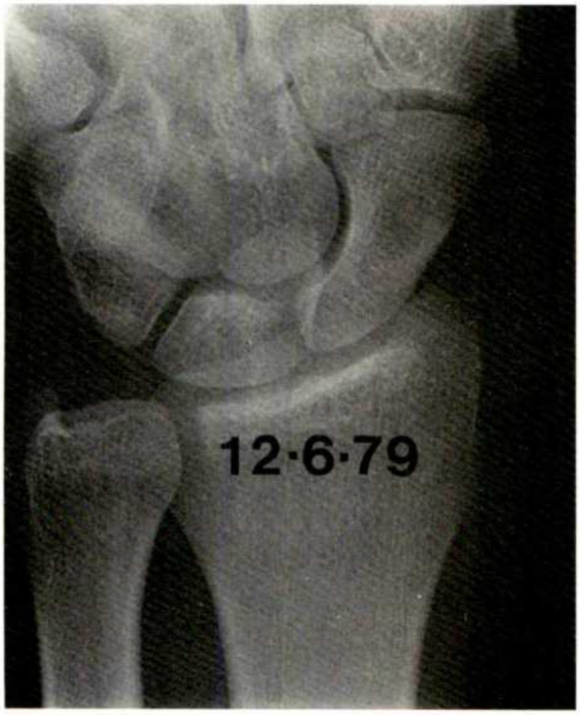


FIG. 1.

Other patterns of AFIU, detected by IBI, involving the radial epiphysis, the radial styloid and capitate, are given in Figs. 4–6. In Fig. 4, which

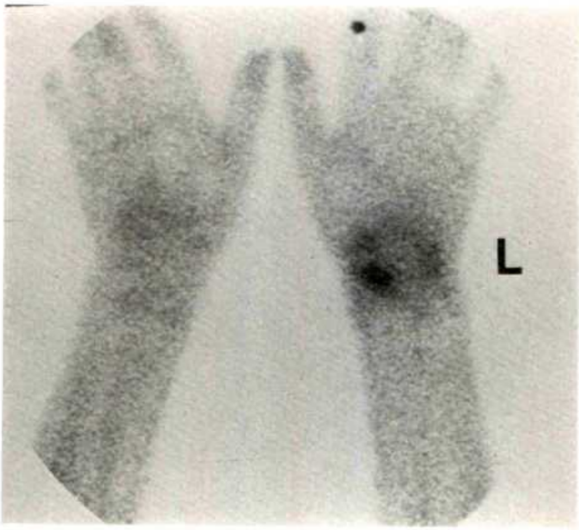


FIG. 2.

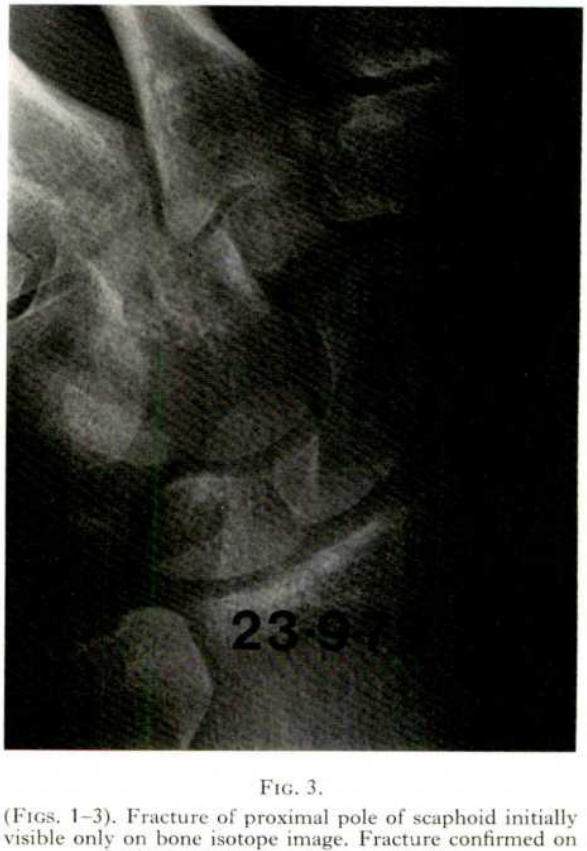


FIG. 3.

(FIGS. 1–3). Fracture of proximal pole of scaphoid initially visible only on bone isotope image. Fracture confirmed on further examination three months later.

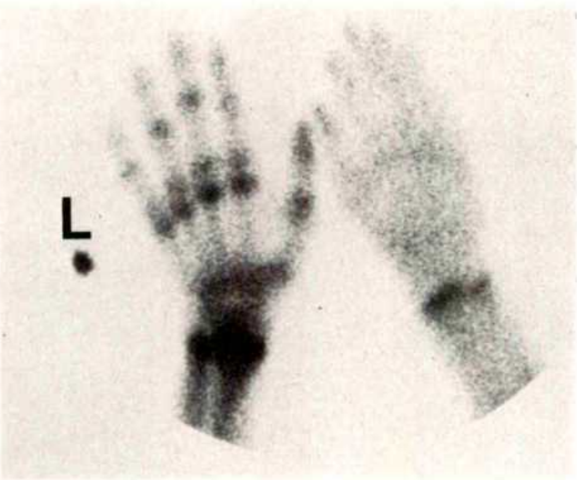


FIG. 4.

Trauma to unfused radial epiphysis, not detected radiographically. Note increased uptake in relation to the epiphyses, possibly due to "sympathetic" increase in blood flow.

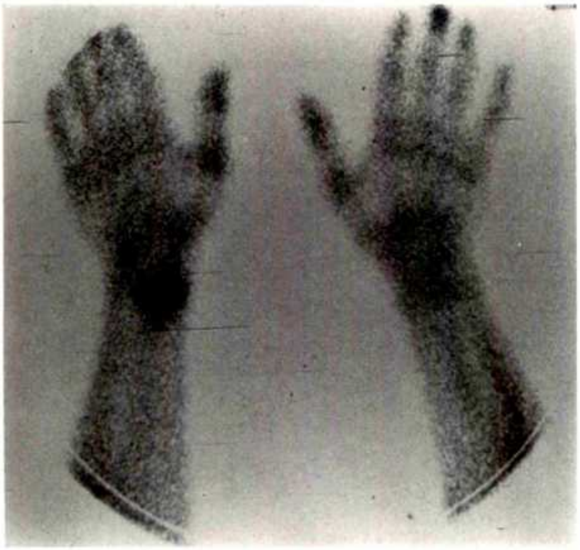


FIG. 5.

Trauma to radial styloid. Fracture confirmed on further radiographic examination.

reveals AFIU in relation to the unfused radial epiphysis of a 13-year-old boy, there is a significant increase in the degree of uptake by the epiphyses of the metacarpals and phalanges, possibly due to a "sympathetic" increase in blood flow.

If imaging is performed within 48 hours of injury it may be difficult to identify an area of AFIU within a generalized increase of isotope distribution within

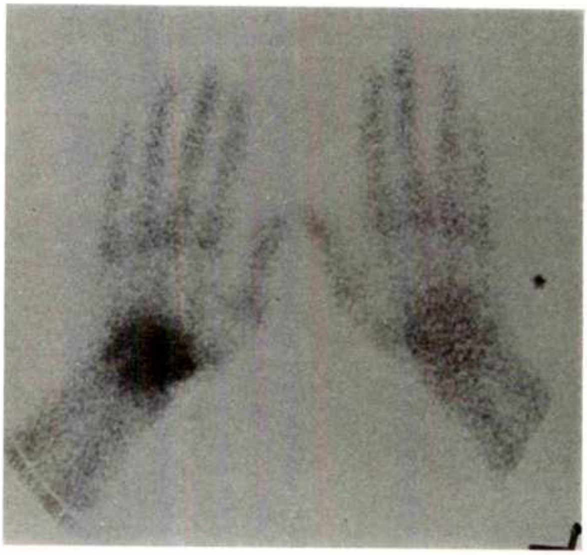


FIG. 6.

Trauma to capitate. Fracture located on X-ray with aid of bone image.

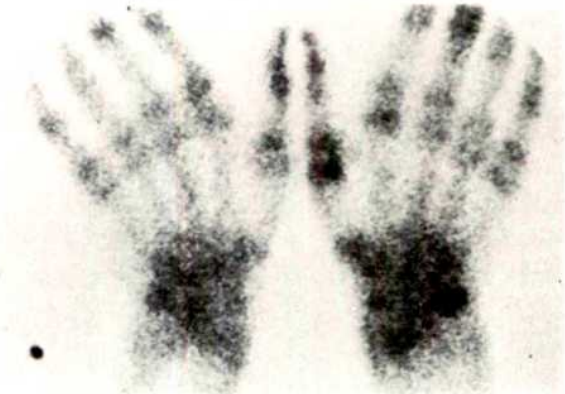


FIG. 7.

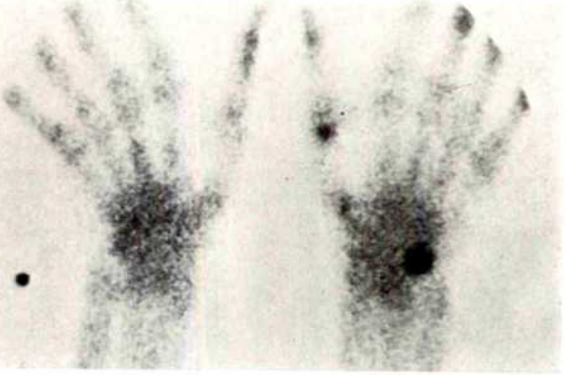


FIG. 8.

(FIGS. 7–8) Triquetral fracture initially obscured by diffuse uptake within carpus, but clearly seen seven days later.

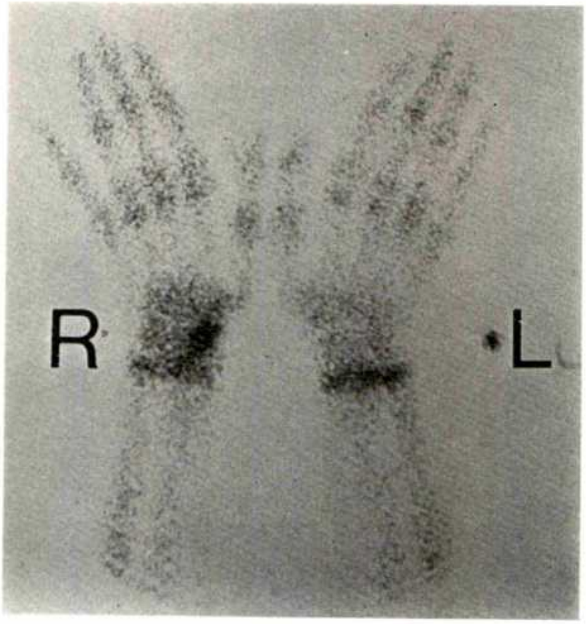


FIG. 9.

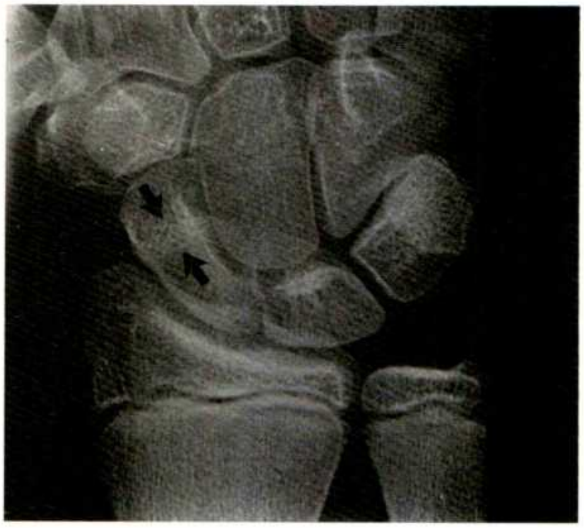


FIG. 10.

(FIGS. 9–10) Old fracture of the scaphoid still positive one year after trauma on bone isotope image.

the carpus secondary to soft tissue injury. This problem may be resolved by IBI seven days later (Figs. 7–8).

Figure 9 shows the results of IBI on a 14-year-old boy with recent left carpal trauma. IBI shows obvious evidence of AFIU in the right scaphoid. On further questioning, the patient confirmed a history of right carpal trauma one year previously. A radiograph obtained at that time was interpreted as normal, but repeat X-ray examination at the time of the isotope bone scan confirmed an old scaphoid fracture (Fig. 10). This case illustrates the frequently persistent positivity of IBI following trauma.

All isotope images were stored on computer for quantitative analysis. In AFIU the mean uptake ratio, compared with the corresponding uninjured side, was found to be 1.95 (SD 0.71). This shows an approximately two-fold increase in isotope uptake at the site of SBT. No clear correlation emerged between the uptake ratio and the interval between trauma and IBI.

DISCUSSION

Initial radiographic examination of the carpus may fail to reveal definite evidence of fracture despite clinical suspicions of such an injury. In these cases, so that missed diagnoses and consequent avascular necrosis or pseudoarthrosis formation (Alho and Kankaanpaa, 1975) may be avoided, it is usual clinical policy to treat these patients as for fracture and repeat radiographic examination at a later date. The proportion of patients who will be shown to harbour a carpal fracture on subsequent radiographic study will depend on the judgement and circumspection of the referring doctor. Some cases will, however, have undergone what in retrospect was an unnecessarily long period of immobilization. This paper explores the part which IBI may play in predicting whether or not osseous injury exists, in order that early definitive diagnosis and treatment of carpal injuries may be instituted.

The addition of IBI to conventional radiography has been shown to facilitate the identification of bone trauma (Fordham and Ramachandran, 1974; Marty *et al.*, 1976; Rosenthall *et al.*, 1976). Traumatic as well as stress fractures have been demonstrated on IBI some weeks before the characteristic radiographic appearances are manifest (Iimori *et al.*, 1975; Prather *et al.*, 1977; Wilcox *et al.*, 1977). The role of IBI in the early identification of scaphoid fractures has been recently examined (Ganel *et al.* 1979; Jørgensen *et al.*, 1979).

In the series of 49 patients which Ganel *et al.* studied, on initial radiographic examination 11 showed a definite scaphoid fracture whilst in 31 cases the appearances were described as doubtful. The remaining seven were considered to have normal radiographs. All of the group of 11 with initial positive radiographic findings of scaphoid fracture were also positive on IBI, while of the 31 doubtful radiographic fractures, six had positive bone scans and 25 were normal. Of the six positive IBI cases, five later showed radiographic evidence of scaphoid fracture.

There are, however, several notable differences between the findings of these two groups of workers (Ganel *et al.*, 1979; Jorgensen *et al.*, 1979) and the results of this present investigation. Criteria on which patients were selected for inclusion in the current trial differed in that a pre-requisite for entry was, in addition to clinical suspicion of a scaphoid fracture, normal initial radiographic examination. Only seven of Ganel's cases fulfil this condition. Of these seven, two were positive on IBI for scaphoid trauma, one of which was positive on subsequent radiographic examination.

In our study 47 patients had AFIU of whom 19 (42%) had subsequent radiological evidence of fracture. Of the 50 areas of AFIU that were shown in these 47 cases, only 52% were related to the scaphoid, whilst 18% occurred within the distal radius, 10% in the trapezoid and 8% within the triquetrum. Such distribution of AFIU was not encountered by Ganel *et al.*, who describe only scaphoid fractures. Of the 24 areas of AFIU demonstrated in bones other than the scaphoid, 10 (41%) showed subsequent radiological evidence of fracture.

The exact aetiology of the AFIU occurring at these sites, as well as those shown in relation to the scaphoid, is uncertain in the absence of subsequent confirmatory radiological evidence of fracture. A localized soft tissue injury involving torn ligaments may be a possible explanation, perhaps in association with adjacent haematoma formation. Such a speculation is, however, difficult to confirm or refute. Periosteal reaction is thought unlikely to account for such AFIU in the absence of any change demonstrated on subsequent radiographic examination. This same objection would also apply to cortical infarction as a cause for AFIU. When examining the radiograph, degenerative joint disease must be diligently sought, since this will result in focal increased uptake on IBI and hence false positive results. Since the average age of the 99 patients in our series was 23 years, degenerative joint disease did not present a significant problem.

In IBI, premature imaging before 48 hours must be avoided to exclude false-negative results. This point is of special relevance in traumatic synovitis or hyperaemia which gives a generalized increase in isotope uptake, obscuring focal uptake at the site of bone injury (Rosenthall *et al.*, 1976).

The current study has revealed AFIU at sites other than the scaphoid in 48% of all cases showing abnormal IBI, a finding which is comparable to the results of Jørgensen *et al.*, who described ten fractures of the wrist in the series of 50 patients which they reported. The distribution of such areas of AFIU seen in our study appears, however, to be wider. This may reflect differences in the method of case selection between the present study and those previously reported (Ganel *et al.*, 1979; Jørgensen *et al.*, 1979). However, since in the current series, all patients were referred because of a clinical suspicion of scaphoid fracture, this finding of AFIU at sites other than the scaphoid is of some interest. As radiological evidence of fracture is clearly seen in 41% of these cases where no radiological signs of a suspected scaphoid fracture are seen, it is essential that a thorough appraisal of the entire carpus and adjacent bones be performed. Fractures were often more easily identified on X-ray examinations with the assistance of IBI. It is also pertinent to note that the conventional radiographic "scaphoid views" may not necessarily show the remainder of the carpus to best advantage.

Although it would be erroneous to assume that a well-localized "hot spot" shown by IBI within the wrist of a patient who has a history of recent carpal trauma is invariably due to a complete fracture which has been overlooked or not demonstrated on radiological examination, IBI can be used confidently to predict the group within which fractures may exist. Those patients who show normal IBI may be spared not only further rigorous clinical and radiographic follow-up, but also unnecessarily protracted periods of immobilization. This could result in economic savings for the individual patient due to an earlier resumption of employment, and also for the hospital service in terms of fewer out-patient and radiographic appointments. Furthermore, the use of IBI confers greater accuracy upon the radiological examination by indicating the precise area of the carpus within which a fracture may possibly be found. In view of the potentially serious implications of overlooking such fracture (Bailey and Love, 1977) it is hoped that IBI may be usefully applied in the future management of such cases.

ACKNOWLEDGMENTS

We are grateful to the radiography staff of the Wessex Regional Department of Nuclear Medicine for their kind assistance during this study and also to Mrs. Margaret Eckersley for typing the final manuscript.

REFERENCES

ALHO, A. and KANKAANPAA, U., 1975. Management of fractured scaphoid bone. *Acta Orthopaedica Scandinavica*, *46*, 743–757.

BAILEY, H. H. and LOVE, R. J. McN., 1977. In *Short Practice of Surgery*, 17th edition, revised by A. J. Harding-Rains and H. D. Ritchie. (H. K. Lewis, London) pp. 341–342.

FORDHAM, E. W. and RAMACHANDRAN, P. C., 1974. Radionuclide imaging of osseous trauma. *Seminars in Nuclear Medicine*, *4*, 411–429.

GANEL, A., ENGEL, J., OSTER, Z. and FARINE, I., 1979. Bone scanning in the assessment of fractures of the scaphoid. *Journal of Hand Surgery*, *6*, 540–543.

IIMORI, M., HISADA, K. and SUSZUKI, Y., 1975. Technetium 99m pyrophosphate bone scanning in the evaluation of trauma (abstract). *Journal of Nuclear Medicine*, *16*, 538.

JAMES, A. G., FRANCIS, M. D. and DAVIS, M. A., 1976. Bone scanning, radionuclide reaction mechanisms. *Seminars in Nuclear Medicine*, *6*, 3–18.

JØRGENSEN, T. M., ANDRESEN, J. H., THOMMESEN, P. and HANSEN, H. H., 1979. Scanning and radiology of the carpal scaphoid bone. *Acta Orthopaedica Scandinavica*, *50*, 663–665.

MARTY, R., DEENEY, J. D., MCKAMEY, M. R. and ROWLEY, M. J., 1976. Bone trauma and related benign disease: assessment by bone scanning. *Seminars in Nuclear Medicine*, *6*, 107–120.

PENDERGRASS, H. P., POTSAID, M. S. and CASTRONOVO, F. P., 1973. The clinical use of 99m-Tc diphosphonate (HEDSPA): a new agent for skeletal imaging. *Radiology*, *107*, 557–562.

PRATHER, J. L., NUSYNOWITZ, M. L. and SNOWDY, H. A., 1977. Scintigraphic findings in stress fractures. *Journal of Bone and Joint Surgery*, *59A*, 869–874.

ROSENTHALL, L., HILL, R. O. and CHUANG, S., 1976. Observation on the use of 99m-Tc phosphate imaging in peripheral bone trauma. *Radiology*, *119*, 637–641.

ROSENTHALL, L. and LISBONA, R., 1980. Role of radionuclide imaging in benign bone and joint diseases of orthopaedic interest. *Nuclear Medicine Annual*. Ed. by L. M. Freeman and H. S. Weissmann (Raven Press, New York), 267–301.

SHARMA, S. M. and QUINN, J. L., 1972. Sensitivity of 18F bone scans in search of metastases. *Surgery, Gynaecology and Obstetrics*, *135*, 536–540.

TOTHILL, P. and MCCORMICK, J. S., 1975. Bone blood flow in rat determined by uptake of bone seeking radiopharmaceuticals and radioactive particles (abstract). *British Journal of Radiology*, *48*, 70.

WILCOX, J. R., Jnr., MONIET, A. L. and GREEN, J. P., 1977. Bone scanning in the evaluation of exercise related stress injuries. *Radiology*, *123*, 699–703.

Book review

Fundamental and Clinical Bone Physiology. Ed. by Marshall R. Urist, pp. xii+416, 1980 (Lippincott, Philadelphia/London), £39·00.

ISBN 0-397-50470-5

Whilst trying to preserve a balance between the basic and the practical as in the title, the former is dominant in the twelve review articles presented in this collection of selected topics in skeletal physiology. Nevertheless, throughout the text much attention has been devoted to indicating the clinical bearing of advances in this field of biological science. Extending beyond the human species, these papers describe the growth of bone and bones, their structure, maintenance, damage and repair together with certain of the commoner bone disorders. This is essentially a book for the individual with a prime interest in the skeleton and offers a fertile medley of biochemistry, morphology and behaviour of bone otherwise dispersed through the pages of rather diverse journals. Some repetition between papers is inevitable when attempting to reconcile molecular data with ultrastructure in one direction, or with clinical and radiological features in the other.

In the study of normal and diseased bone several major difficulties arise, as may be exemplified briefly by bone growth. From the first minute speck of ossification in the embryo to its final maturation, bone growth is subject to multifactorial controls some genetic, some environmental. To a large degree heritable factors are still obscure, although more clearly understood in connection with growth than in their relevance to bone disease. In investigating the environmental aspects of bone physiology it is usually necessary to move one step at a time, *e.g.* effects of Vitamin D on bone, although *in vivo* this is but one compound amongst many intimately concerned either simultaneously or sequentially with bone growth and metabolism. The results of oversimplified experiments may thus be misleading and provide concepts which flounder in a morass of controversy. Thus, for example, despite five decades since the classic work of Robison, the role of alkaline phosphatase in bone mineralization is still uncertain.

With these caveats this book provides a wealth of up-to-date information on skeletal tissues supplemented by chapters on fracture repair, bone grafting and heterotopic ossification of soft tissues. Particularly valuable are the papers by Triffitt on the organic matrix of bone, by Ogden on chondro-osseous growth and by Simmons on fracture repair.

Naturally, one reflects on the value of this book to those engaged in radiology, radiotherapy and closely allied specialities. The declared coverage is for "students and new research workers" and "readers preparing for a career in either basic science or one of the applied clinical specialities". It is not likely to appeal greatly to the great majority of the radiological heirarchy, whether diagnostic or therapeutic; but could well be of importance for the radiobiologist, for the oncologist occupied with chemotherapy and nuclear medicine. for the paediatric radiologist or anyone concerned with radiodiagnosis of fractures or metabolic and heritable bone disorders. For the radiotherapist it is disappointing that little is included about post radiation bone changes or the effects of primary or metastatic cancer upon bone. But many would read some part with profit, whilst to a few the whole would be rewarding and stimulating.

The volume has a convenient format with a competent subject index. The present writer would strongly contest occasional bold statements in the text *e.g.* "The osteoblast apparently is not capable of cell division" (p. 123)—when mitoses in such cells are not hard to find! There is a modest crop of printing errors with mistakes in the legends to several figures. Moreover, it is a pity that reproductions of photomicrographs do not always state the stain and magnification. The photolithographic method of printing may sometimes blur the definition in electron micrographs and photomicrographs, and give a monotonous tone to their image. In view of the rather prevalent abbreviations (some quite unfamiliar) a glossary of these and other less common terms would have been a useful adjunct.

Clearly, this book will be appreciated mainly by those preoccupied with the skeleton irrespective of their particular job.

C. H. G. PRICE.

1981, *British Journal of Radiology*, *54*, 768–772

A study of the effect of sodium/meglumine ioxaglate (Hexabrix) on thyroid function

By R. G. Grainger, M.D., F.R.C.P., F.R.C.R.
Department of Radiodiagnosis, Royal Hallamshire Hospital, Sheffield, S10 2JF
and G. W. Pennington, M.D., M.Sc., F.R.C.Path.
Sheffield and Region Endocrine Investigation Centre, Jessop Hospital for Women, Sheffield S3 7RE

(*Received March 1981*)

ABSTRACT

The effect on thyroid function was investigated in 22 patients undergoing arteriography with a new low osmolality contrast medium—sodium and meglumine ioxaglate (Hexabrix). Plasma thyroxine (T4), thyroxine resin uptake (TRU) and free thyroxine index (FTI) were measured before and at varying intervals up to 56 days after the arteriogram. Despite the large doses of Hexabrix used (up to 89.6 g of iodine), these tests of thyroid function did not reveal any significant change from pre-angiographic levels. It is concluded that Hexabrix as used for arteriography does not affect thyroid function.

The present study was designed to investigate whether thyroid function is modified by massive doses of iodine, delivered directly into the circulation in the form of a new radiological contrast medium—sodium and meglumine ioxaglate (Hexabrix).

The normal daily turnover of iodine within the body is about 70 μg. Patients undergoing radiological examination of the vascular tree are injected with very high doses of iodine, *e.g.*, Patient No. 12 in this series received 89.6 g of elemental iodine in 90 min, *i.e.* 1 280 000 times the normal 24-h body turnover.

As the thyroid gland and its hormones contain almost all of the iodine in the body, it might be expected that this massive dose of iodine could alter thyroid function.

THE CONTRAST MEDIUM

Hexabrix, the contrast medium under investigation, is a 59.4% w/v solution of a 2:1 mixture of the meglumine and sodium salts of a newly synthesized acid—ioxaglic acid (Fig. 1). This acid is a mono-acid dimer and consists of two benzene rings to each of which are attached three atoms of iodine. One molecule of the salt in solution dissociates into one cation (sodium or meglumine) and one anion (the ioxaglate radical containing six atoms of iodine).

Hexabrix contains 320 mg iodine/ml. It has an osmolality of 580 mosmols/kg water, *i.e.* about 40% that of conventional contrast media such as Conray 280, despite the 14% increase in iodine content of Hexabrix. Because of this reduced osmolality, Hexabrix has major clinical advantages over conventional contrast media (Grainger, 1979).

Hexabrix is the registered name of Laboratoire Guerbet (Paris) who synthesised ioxaglic acid. It will be marketed in the UK by May & Baker Ltd.

THE PATIENTS

Twenty patients (12 males, 8 females) age range: 36–76 years (mean ±S.D.=58.65±11.41) had a single angiographic study (Table I). Two further male patients (34 and 71 years) underwent more than one arteriogram during the study period (Table IA). These two patients are excluded from Table II.

METHODOLOGY

Twenty-two patients requiring arteriography were selected for the study. None of the patients had a previous history or current signs or symptoms of thyroid disease. No patient had a goitre. Samples of blood for the estimation of plasma thyroxine (T4), thyroxine resin uptake (TRU) and free thyroxine index (FTI) were taken immediately prior to arteriography. Further blood samples were taken between one and 56 days after the arteriogram, and similar estimations were carried out on these samples.

The angiographic procedures undertaken and the volume of Hexabrix (sodium/meglumine ioxaglate) used for each of the 22 patients investigated are shown in Tables I and IA. The time intervals between the subsequent blood samples and the values of T4, TRU and FTI are also shown in Tables I, IA and II.

Thyroxine (T4) was estimated by the method of Ratcliffe *et al.* (1974) with modifications as described by Pennington *et al.* (1981).

Thyroxine resin uptake (TRU) was measured by the Radiochemical Centre Amersham Kit method as modified by Pennington *et al.* (1981).

The Free Thyroxine Index (FTI) was derived mathematically from the two previous estimations as described by Clark and Brown (1970).

TABLE I

SERUM T4, THYROID RESIN UPTAKE AND FREE THYROXINE INDEX FOLLOWING ANGIOGRAPHY WITH HEXABRIX

			T4 (nmol/l)						Thyroid resin uptake (nmol/l)						Free thyroxine index (nmol/l)					
				Time of sample following angiography						Time of sample following angiography						Time of sample following angiography				
Patient No. Age/Sex	Procedure	Volume of Hexabrix used	Pre-angiography	0–3 days	4–7 days	8–14 days	15–28 days	29–56 days	Pre-angiography	0–3 days	4–7 days	8–14 days	15–28 days	29–56 days	Pre-angiography	0–3 days	4–7 days	8–14 days	15–28 days	29–56 days
1. 54/M	Carotid arteriography	50 ml	69	75		76		79	104	97		103		102	66	77		73		77
2. 51/F	Carotid arteriography	50 ml	60	66				104	84	90				107	71	73				97
3. 43/F	Carotid arteriography	50 ml	87	83		62		58	100	99		95		99	87	83		65		58
4. 74/M	Carotid arteriography	40 ml	85	74					105	104					80	71				
5. 63/M	Carotid arteriography	30 ml	101	101				85	103	105	105			102	98	96				83
6. 70/M	Carotid arteriography	50 ml	48	52	65				100	95	96				48	54	67			
7. 76/F	Carotid arteriography	60 ml	69	67					102	107					67	62				
8. 54/M	Carotid arteriography	50 ml	104			104			101			96			102			108		
9. 41/F	Carotid arteriography	52 ml	73	89		111		81	101	101		92		106	72	85		120		76
10. 58/M	Carotid +vertebral arteriography	100 ml	87	89			73		103	109			103		84	81			70	
11. 57/F	Carotid arteriography +abdominal aortography	250 ml	88	85		108		81	89	98		96		100	98	86		112		81

Normal values: T_4 = 60–170 nmol/l; Thyroid resin uptake = 86–110 nmol/l; Free thyroxine index = 60–170 nmol/l.

TABLE Ia

Details of patients undergoing more than one angiogram with Hexabrix during the study period

Patient No. Age/Sex	Procedure (angiography No.)	Time interval between angio-grams	Volume of Hexabrix used	T4 (nmol/l)						Thyroid resin uptake (nmol/l)						Free thyroxine index (nmol/l)					
				Pre-angio-graphy	Time of sample following angiography					Pre-angio-graphy	Time of sample following angiography					Pre-angio-graphy	Time of sample following angiography				
					0–3 days	4–7 days	8–14 days	15–28 days	29–56 days		0–3 days	4–7 days	8–14 days	15–28 days	29–56 days		0–3 days	4–7 days	8–14 days	15–28 days	29–56 days
21. 34/M	Hepatic (1) arteriography + abdominal aortography		110 ml	87	68			65		94	94			100		92	72			65	
	Hepatic (2) arteriography	28 days	50 ml	74						75						98					
	Coeliac+ (3) hepatic+ splenic arteriogram	28 days	150 ml	63	50			59	54	92	97			98	99	68	51			60	53
22. 71/M	Renal (1) arteriography		120 ml	102	98					94	88					108	111				
	Renal (2) venogram + inferior vena cava venogram	28 days	140 ml	104	126			84		96	101			79	9	108	124			106	

Normal values: T_4 = 60–170 nmol/l; Thyroid resin uptake = 86–110 nmol/l; Free thyroxine index = 60–170 nmol/l.

Results

Thyroxine (T4)

All of the pre-angiography T4 basal values were within the laboratory normal range (60–170 nmol/l) with one exception (Patient 6) who had a basal value of 48 nmol/l.

Following intravascular injections of Hexabrix, at a dose varying between 50 ml and 280 ml, values of T4 concentration at various time intervals were observed both to rise and fall, with a fairly uniform scatter of results. Making a comparison between the pre-angiography level and the subsequent highest and lowest recorded value, the T4 concentration fell in 12 patients, rose in seven and remained the same in one.

Observations of the mean and standard deviation figures (Table II) demonstrates that in all instances the mean values following Hexabrix angiography fell within the 1SD range (69.04–106.96), indicating that these values are not significantly different from the pre-angiography range.

The coefficient of variation for the assay is of the order of 7%. Application of Student's '*t*' test demonstrated no significant difference between the pre-angiography and the highest T4 post-angiography T4 level (*t* value = 1.192 with 23 degrees of freedom).

Concentrations above and below the normal range are sometimes encountered in the absence of thyroid dysfunction, and are usually due to changes in the level of serum thyroid binding globulin. This may be either congenital or acquired, the latter being associated with a variety of non-thyroid illnesses or with the ingestion of some drugs. There is a tendency to lower concentrations of T4 after the age of 65, while mean values in females tend to be about 5% higher than in males. The two patients in Table Ia are not included in Table II. Their tests of thyroid function show no disturbance even after more than one arteriogram.

Thyroid Resin Uptake (TRU)

Following administration of Hexabrix there was a scatter of results. In eight patients there was a fall in thyroid resin uptake, in eight a rise, while in four the results were equivocal. Scrutiny of Table II indicates that the pre-angiography values are all within the 1 SD range of 93.34% to 105.96% (99.65±6.31). All post-Hexabrix values were within this range, indicating that the two groups did not significantly differ. Application of Student's '*t*' test demonstrated no significant difference between the pre-angiography and the highest TRU post-angiography level (*t* value = 2.380 with 23 degrees of freedom).

TABLE II

Timing of samples, range and mean of values of T4, thyroid resin uptake and free thyroxine index

Investigation + normal range	Time of test	No. of patients	Range of values n.mol/l	Mean ± SD of range
T4 60–170 nmol/L	Pre-angiography	20	60–121	mean = 88 SD ± 18.96
	0–3 days	18	52–108	mean = 85.22 SD ± 16.28
	4–7 days	2	65–94	mean = 79.5 SD ±
	8–14 days	7	62–111	mean = 90.71 SD ± 18.50
	15–28 days	4	73–108	mean = 87.5 SD ± 15.63
	29–56 days	9	58–104	mean = 83.78 SD ± 13.57
Thyroid resin uptake 86–110 nmol/L	Pre-angiography	20	84–108	mean = 99.65 SD ± 6.31
	0–3 days	18	90–109	mean = 100.11 SD ± 5.43
	4–7 days	3	96–105	mean = 102 SD ±
	8–14 days	7	92–105	mean = 98.85 SD ± 5.34
	15–28 days	4	102–105	mean = 103.5 SD ± 1.29
	29–56 days	9	99–107	mean = 103.11 SD ± 2.93
Free thyroxine index 60–170 nmol/L	Pre-angiography	20	48–121	mean = 88.05 SD ± 19.20
	0–3 days	18	54–114	mean = 84.77 SD ± 16.54
	4–7 days	2	67–89	mean = 78 SD ±
	8–14 days	7	65–120	mean = 91.86 SD ± 21.58
	15–28 days	3	70–103	mean = 77.33 SD ±
	29–56 days	10	58–97	mean = 83 SD ± 13.21

This test measures the unoccupied thyroid-hormone binding sites on thyroid binding globulin (TBG). Performed *in vitro* using T3 or T4 labelled with radio-iodine and ion-exchange resins, the proportion of radioactive hormone that is not tightly bonded to the serum protein is measured. The results are expressed as a percentage of the result obtained in a normal control serum run in the same assay as the test sample. The range of normal values is 86–110%.

Free Thyroxine Index (FTI)

Scrutiny of Table II indicates no significant differences before and after the administration of Hexabrix.

Application of Student's '*t*' test demonstrated no significant difference between the pre-angiography and the highest FTI post-angiography level (*t* value $=0.997$ with 23 degrees of freedom).

The free thyroxine index is the most convenient method for the estimation of free thyroxine in serum. The index is mathematically derived using data from the thyroxine (T4) level and the *in vitro* thyroid resin uptake test (TRU). As both these latter estimations are similar both before and after Hexabrix, differences in the free thyroxine index would not be expected.

Discussion

The administration of large doses of iodine causes very complex, seemingly contradictory and often variable effects on thyroid function. Acute but short-lived inhibition of thyroid hormone release has been well described in thyrotoxic patients. Braverman *et al.* (1969) have also documented a sustained inhibition of thyroid hormone synthesis. On the other hand, Alexander *et al.* (1965) found an increased iodine uptake and relapse of thyrotoxicosis in some treated thyrotoxic patients. The general consensus of opinion indicates, however, that thyroid hormone secretion remains constant despite wide fluctuations in iodine supply (Vagenakis *et al.*, 1973; Studer *et al.*, 1974).

Following intravascular injection of radiological contrast media, Clark and Shipley (1957) and Grayson (1960) demonstrated a depression in thyroidal radio-iodine uptake. Davis (1966) found an elevation of plasma protein bound iodine after contrast medium administration.

Burgi *et al.* (1976) suggested that significant changes in circulating levels of thyroid hormones (decrease in T3 with parallel rise in reverse T3 and T4) were frequently found following the use of oral cholecystographic iodinated contrast media. Hanaghan *et al.* (1979) investigated 31 patients, all euthyroid (but 11 had a non-toxic goitre) after contrast medium administration. They utilized two different types of contrast medium—28 patients received an oral cholecystographic agent, iopanoic acid (Telepaque), and only three patients received intravascular diatrizoate (Urografin). These two drugs have very different pharmacokinetics, *e.g.*

iopanoic acid has a much longer half-life and is more readily bound to protein than diatrizoate. Burgi *et al.* (1976) found considerable difference in thyroid function following urographic as compared with cholecystographic contrast media. Unfortunately, the results for these two different contrast media are not presented separately by Hanaghan *et al.* (1979) who found an early (three-day) rise in serum reverse tri-iodothyronine (RT3) with a parallel rise in serum thyroxine (T4) level. After three weeks, the serum tri-iodothyronine (T3) levels were significantly greater than base values. These results are in close agreement with those of Burgi *et al.* (1976) following oral cholecystographic contrast media.

The effects of Hexabrix (the contrast medium utilized in the present study) on many parameters of thyroid function have also been studied by Jaffiol and Baldet (1980). They were able to demonstrate a minimal decrease in plasma thyroxine level (T4) at 48 hours when compared with pre-injection levels. All variations reported were minimal and did not exceed physiological values. TRU and FTI levels were not measured. Jaffiol and Baldet (1980) concluded that their results do not differ from those of Burgi *et al.* (1976) who noted no variation in T4, T3 and reverse T3 levels in subjects given an intravenous urographic iodinated contrast medium (as compared with changes found following oral cholcystographic agents).

In the present study, 22 patients were investigated for thyroid function up to 56 days following Hexabrix arteriography. No consistent rise or fall in T4, TRU or FTI values were observed. There would appear to be no variation in the unoccupied thyroid-hormone binding sites on thyroid binding globulin. In view of our inability to demonstrate any influence on tests of thyroid function after very large doses of intra-arterial Hexabrix (up to 89.6 g iodine), it is concluded that this new intravascular radiological contrast medium does not affect thyroid function. The six atoms of iodine of each molecule of Hexabrix must be extremely firmly bonded to the two benzene rings.

ACKNOWLEDGMENTS

It is a pleasure to acknowledge the assistance we have received from the staff of the Radio-diagnostic Department of the Royal Hallamshire Hospital and of the Sheffield and Region Endocrine Investigation Centre, Jessop Hospital for Women, Sheffield.

The supplies of Hexabrix were kindly provided by May & Baker Ltd., Dagenham, Essex and we wish to thank Miss Barbara Bushell and Mr. A. Crichton of that company for their help with this study.

REFERENCES

Braverman, L. E., Woeber, K. A. and Ingbar, S. H., 1969. Induction of myxoedema by iodine in patients euthyroid after radioiodine or surgical treatment of diffuse toxic goitre. *New England Journal of Medicine, 281*, 816–821.

Burgi, H., Wimphreimer, C., Burger, A., Zaunbauer, E., Rosler, H. and Lemarchand-Berand, T., 1976. Changes in circulating thyroxine, triiodothyronine and reverse triiodothyronine after radiographic contrast agents. *Journal of Clinical Endocrinology and Metabolism, 43*, 1203–1210.

Clark, F. and Brown, H. J., 1970. Free thyroxin index. *British Medical Journal, i*, 713–715.

Clark, R. E. and Shipley, R. A., 1957. Thyroidal uptake of I^{131} after iopanoic acid (Telepaque) in 74 subjects. *Journal of Clinical Endocrinology and Metabolism, 17*, 1008–1010.

Davis, P. J., 1966. Factors affecting the determination of the serum protein bound iodine. *American Journal of Medicine, 40*, 918–940.

Grainger, R. G., 1979. A clinical trial of Hexabrix. *British Journal of Radiology, 52*, 781–786.

Grayson, R. R., 1960. Factors which influence the radioactive iodine thyroidal uptake test. *American Journal of Medicine, 28*, 397–415.

Hanaghan, J., Dhupella, D. and Finucane, J., 1979. Thyroid hormones in serum: effects of X-ray contrast media. *Irish Journal of Medical Science, 148*, 12–14.

Jaffiol, C. and Baldet, L., 1980. Private communication to Laboratoire Guerbet, 93601 Aulnay-sous-Bois, Cedex, France.

Pennington, G. W., Naik, S. and Bevan, B. R., 1981. In *The Thyroid Gland in Hormonal Analysis—Methodology and Clinical Interpretation.* Ed. by G. W. Pennington and S. Naik (C.R.C. Press, Boca Raton, Florida, USA) (in press).

Ratcliffe, W. A., Ratcliffe, J. G., McBridge, A. D., Harland, W. A. and Randell, T. W., 1974. The radioimmunoassay of thyroxin in unextracted plasma. *Clinical Endocrinology, 3*, 481–488.

Studer, H., Kohler, H. and Burgi, H., 1974. Iodine deficiency—In the thyroid. *American Physiological Society Handbook Series.* (Ed. by D. H. Solomon and M. A. Greer) Vol. III, Section 7, pp. 303–328.

Vagenakis, A. E., Downs, P., Braverman, L. E., Burger, A. and Ingbar, S. H., 1973. Control of thyroid hormone secretion in normal subjects receiving iodides. *Journal of Clinical Investigation, 52*, 528–532.

1981, *British Journal of Radiology*, *54*, 773–781 SEPTEMBER 1981

New modalities in cancer treatment: heavy charged particles[*][†]

By E. J. Hall, M.A., D.Phil., D.Sc.

Radiological Research Laboratory, Columbia University College of Physicians and Surgeons,
New York, New York 10032, USA

(*Received January 1981*)

ABSTRACT

Heavy charged particles represent the ultimate that the physicist can contribute to the development of radiation sources for therapy.

Of the heavy charged particles, protons are the least expensive to accelerate and can be manipulated to give a sharply defined high-dose volume with a rapid fall-off of dose outside the target area. The biological properties of protons do not differ significantly from X or γ rays.

Negative pi mesons require an elaborate accelerator for their production. Pions offer the possibility of concentrating energy, some of it densely ionizing with a reduced oxygen enhancement ratio and elevated biological effectiveness within the designated tumour volume, while minimizing the dose of sparsely ionizing radiation to the normal tissues traversed.

High-energy heavy ions offer the greatest flexibility and allow localized dose distributions and also, with the higher Z particles, a substantial reduction of the oxygen enhancement ratio can be achieved.

The ultimate choice of particle depends upon what turns out to be the most important factor in radiotherapy—an improved localization of dose or a reduction in the dependence of cell killing on the presence of molecular oxygen.

Charged particles represent the ultimate that the physicist can contribute to the improvement of dose distribution in radiation oncology. The results of therapy with photons have improved substantially in the past 30 years. Much of this advance is attributed to improvement of the physical dose distribution resulting from the development and introduction of megavoltage sources, principally ^{60}Co teletherapy units and linear accelerators. It must be admitted that few, if any, controlled clinical trials have been performed to document this improvement, much less its cause, but it is a reasonable and widely held impression. The next logical step in this direction would be the introduction of accelerated heavy charged particles. The candidates at present include:

1. Protons.
2. Negative pi mesons (pions).
3. High-energy heavy ions (carbon, neon and argon).

The relative masses of these particles compared with the electrons set in motion when X-ray photons are absorbed are illustrated in Fig. 1. Pions have a mass about 273 times that of an electron or about one-sixth that of a proton, while carbon, neon and argon have mass numbers of 12, 20, and 40 respectively.

As major new modalities in experimental radiotherapy, heavy charged particles must compete directly with neutrons as well as with hypoxic-cell radiosensitizers. The extent to which this competition is simple and direct, or complex and indirect, is illustrated in Fig. 2. The rationale for hypoxic cell sensitizers is based entirely on their ability to increase the radiosensitivity of hypoxic cells which otherwise may be intransigent to killing by X rays. The original rationale for neutrons was also based on the oxygen effect, inasmuch as the cell killing effect of neutrons is less dependent on the presence or absence of molecular oxygen than is the case for X rays (Fowler *et al.*, 1963). However, neutrons differ from X rays in other ways too, including the amount of sublethal damage they produce; this may constitute an advantage or disadvantage for neutrons depending on whether normal or tumour cells are

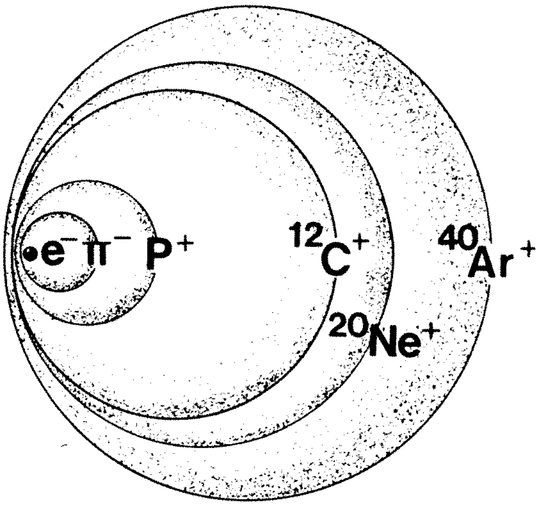


FIG. 1.

Illustrating the relative masses of heavy charged particles compared with a secondary electron set in motion by the absorption of an X-ray photon.

---

[*] Based on a paper presented in a Symposium entitled "New Modalities in Cancer Treatment" at The British Institute of Radiology Annual Congress, April 17–18, 1980 at the Royal Free Hospital, London.

[†] This investigation was supported by Contract DE-ACO2-78EVO4733 from the Department of Energy and by Grant Nos. CA-12536 and CA-18506 to the Radiological Research Laboratory/Department of Radiology, and by Grant No. CA-13696 to the Cancer Center/Institute of Cancer Research, awarded by the National Cancer Institute, DHHS.

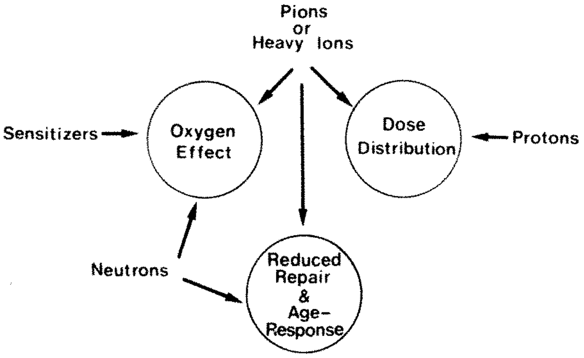


Fig. 2.

The problems addressed by the various new modalities used or proposed for clinical radiotherapy. Electron affinic radiosensitizers are based on the need to reduce the oxygen effects; protons improve the dose distribution; the use of neutrons is based on a reduced oxygen effect, a reduction of sublethal damage repair and reduced age-response function; pions and heavy ions address all three problems.

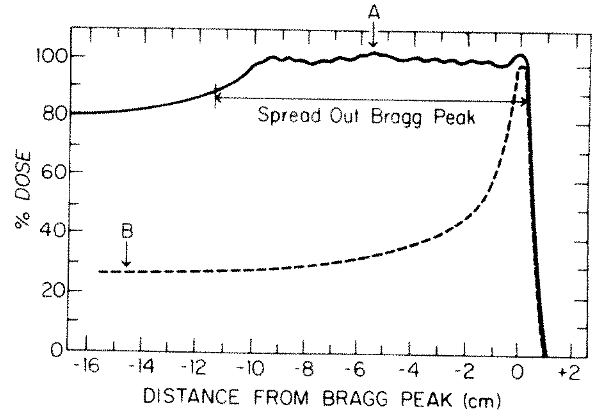


Fig. 3.

Depth-dose distribution for the 160 MeV proton beam generated at the Harvard cyclotron. Curve B shows the sharply defined unmodulated Bragg peak; Curve A shows the distribution used for broad beam radiotherapy with the Bragg peak spread out over 10 cm by the use of a rotating ridge filter of varying thickness.

most efficient at repairing sublethal damage. Whatever the pros and cons of this argument, the degree of accumulation of sublethal damage is different for X rays and neutrons, and has been evoked as a rationale for neutron therapy, particularly by the group in the Netherlands (Broerse and Barendsen, 1973). In addition, the age-response function, *i.e.*, the variation of cellular radiosensitivity for various phases of the cell cycle, is less for neutrons than for X rays, but there is no general agreement as to whether or not this constitutes a significant advantage (Sinclair, 1968; Hall, 1969; Withers *et al.*, 1974).

The various heavy charged particles address different problems too. Protons offer the possibility of a greatly improved dose distribution, while exhibiting biological properties that are indistinguishable from conventional X rays (helium ions are essentially similar to protons—their biological properties may be slightly different, but the difference is of little importance). By contrast, both pions and heavy ions result in changed radiobiological properties as well as allowing an improved dose distribution. They result in a reduced oxygen effect, reduced sublethal damage and age-response function as well as the possibility of improved localization of dose.

All of the high-energy heavy charged particles share the property of improved dose localization because of the way in which they are absorbed. Charged particles stop after penetrating tissue to a depth that depends on their initial energy, delivering a dose that increases with depth very slowly at first while the particles are relativistic, but rising to a sharply defined Bragg peak near the end of their range. By modulating the energy of a particle beam, or interposing a moving ridge filter of variable thickness, this Bragg peak can be spread out or scanned to cover precisely a tumour of a particular size situated at any depth. This ideal can be achieved to varying degrees with the various types of heavy charged particles.

Protons

Protons are by far the least expensive of the heavy charged particles. Their biological properties are indistinguishable from photons (their RBE is about equal to that of 250 kV X rays and perhaps 15% higher than ^{60}Co γ rays). Their attraction is the possibility of a more localized dose distribution, with the expectation of less morbidity for a given dose, or a higher dose for the same morbidity. There is also the possibility of avoiding critical structures in special situations in a way that would never be possible with X rays, because of the sharply defined range of protons. Figure 3 shows the sharp Bragg peak characteristic of the proton beam at the Harvard cyclotron, and the way in which it can be spread out to cover a volume uniformly by the use of a moving filter of variable thickness. Helium ions are essentially similar—they are used extensively at Berkeley because of the availability of a suitable accelerator—but their properties are so similar to protons that it would make little sense to build an accelerator *de novo* for helium ions rather than protons because of the substantially higher cost. Table I lists the principal facilities in the world where protons and helium ions are available. Both protons and helium

TABLE I

PROTON AND HELIUM ION FACILITIES FOR CLINICAL USE

Location	Type of machine	Maximum machine energy (MeV)	Energy to be used clinically (MeV)
Protons			
Harvard, Mass. (USA)	Cyclotron	160	160
Uppsala, Sweden	Synchrocyclotron	187	187
Dubna, USSR	Synchrocyclotron	680	90–200
Moscow, USSR	Synchrotron	7200	70–200
Gatchina, near Leningrad, USSR	Synchrocyclotron	1000	—
Helium ions			
Berkeley, Cal. (USA)	Synchrocyclotron		910
SREL, Newport News, Virginia (USA)	Synchrocyclotron		710
Saclay, France	Synchrocyclotron		645

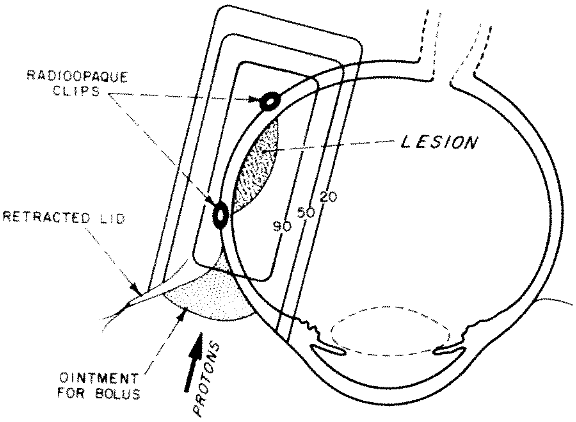


FIG. 4.

Typical dose distribution used for the treatment of choroidal melanoma by the proton beam generated at the Harvard cyclotron. Note the tightly localized high-dose region and rapid fall-off of dose (Courtesy of Dr. Herman Suit, Massachusetts General Hospital and The Harvard Cyclotron).

ions appear to show some selective advantage in certain tumour sites where improved dose localization is critical. Choroidal melanoma is the most obvious example, but there are other selected sites in the head and neck region, particularly about the base of the skull and cervical spine, as well as other anatomical sites of tumours such as soft tissue sarcomata, where improved dose localization would appear to offer a clinical advantage. It is unfortunate that the small number and diversity of the patients treated make it difficult to translate a clinical impression into a statistically valid conclusion.

At the Harvard cyclotron, choroidal melanoma has been treated entirely by proton beam techniques. The results are judged at present to be so striking that it does not appear that controlled clinical trials are needed at this time (Gragoudas *et al.*, 1978; Suit *et al.*, 1977, 1980). Figure 4 shows a typical dose distribution employed for this specialized application which could clearly not be equalled by conventional modalities. This is a special situation where the tight dose distribution and sharp cut-off can be fully exploited. Apart from this site, few patients have been treated with protons alone, the more general use being as a boost for photon therapy of head and neck tumours. Many other sites are barred because of range limitations. The energy of the Harvard cyclotron is 160 MeV, which results in a maximum range of 15.9 cm; it is estimated that an energy of 240 MeV would be needed in a proton accelerator purpose-built for radiotherapy, in order to be able to reach the most deep-seated tumours. In practice, skin reactions are a problem with protons, but this is overcome by combining protons with X rays. Corrections for tissue heterogeneity are much more critical than for X rays and demand a substantial technical effort including the routine use of CT scanning in treatment planning. Using protons, vital structures can be avoided and more localized high-dose areas can be achieved. In the experience at Harvard, marginal misses have not been a problem, even though tighter dose distributions have been employed. The experience with helium ions at Berkeley has been essentially similar. In this case, there is no range limitation because of the high energy of the machine, and one of the sites treated frequently with some success has been carcinoma of the pancreas.

PIONS

The possibility of using pions for radiotherapy has excited basic scientists and clinicians alike ever since their use was first suggested by Fowler and Perkins (1961). Their basic properties would appear ideal for radiotherapeutic applications. High-energy pions behave like overweight electrons while relativistic and exhibit biological properties differing little from X or γ rays. As they slow down near the end of their range, however, pions may be captured by atoms of the absorbing tissue, cascade down the electron energy levels and cause the nucleus to explode into short-range, densely-ionizing fragments which include neutrons and alpha particles; this is the so-called "star production". The narrow Bragg peak of the Los Alamos pion beam is shown in Fig. 5. Not only is the dose high in this peak region, which can be located at any desired depth by choosing particles of the appropriate energy, but the radiation in the peak region has a high LET component and is characterized by an elevated RBE which further increases the ratio of effective dose in the Bragg peak relative to the plateau, and a lowered OER. In practice the Bragg peak must be spread out to cover a tumour of realistic dimensions, and consequently the high LET radiation of the peak is greatly diluted by low LET radiation of the plateau. Figure 5 also illustrates the 10 cm spread-out Bragg peak used for radiotherapy at Los Alamos; of the fragments produced in the "stars", neutrons have a much longer range than the heavier charged particles, and consequently about 10% of the dose in the spread-out Bragg peak is due to neutrons. The biological properties of the spread-out Bragg peak are diluted in proportion to the dilution of the high LET radiation. For example, the OER has been measured to be 2 to 2.2, compared with about 3 for X rays and 1.6 for neutrons (Hall and Astor, 1979; Raju *et al.*, 1979). The RBE of the spread-out peak is in the region of 1.5 to 2 (Yuhas *et al.*, 1979; Raju *et al.*, 1979).

Pions offer the twin advantages of an improved dose distribution compared with X rays and the biological properties of a mixture of high and low LET radiations. The edges of the beam and the end of the range are not as sharp or as clearly defined for pions as for protons, while the OER is not as low as for neutrons, but both advantages are combined in a single beam. The drawback is that large and expensive accelerators are required to produce pions for radiotherapy. Even then the dose-rates may be low and in many cases a limiting factor. This is true at SIN and at Vancouver where radiotherapy with the pion beam is impractical without a sophisticated cryogenic focusing device to collect pions from a large solid angle (known as a piotron). Only at Los Alamos is the dose-rate adequate without such a device. The maximum dose-rate available at present is about 15 cGy (rad)/min to a treatment volume of one litre, which corresponds to a beam current of 600 μA in the accelerator. The Los Alamos accelerator is half a mile in length and accelerates protons to 800 MeV, which are then used to generate pions. The first cancer patient was treated with pions in October 1974 (Kligerman *et al.*, 1977). Since then more than 175 patients have been treated up to November 1980 using the most elegant and sophisticated treatment-planning techniques available. A spectrum of tumour types has been treated including head and neck tumours, gliomas and carcinomas of the prostate, pancreas, rectum and bladder. No definitive results are available from controlled clinical trials, but for some particular cases clinical impressions are very favourable, although it is not clear whether it is the improved dose localization or

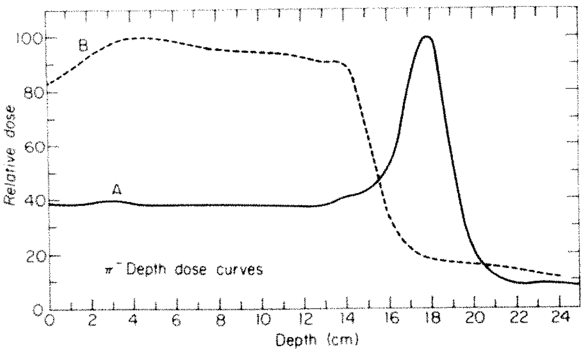


FIG. 5.

Depth-dose curves for negative pi mesons generated at the Los Alamos Scientific Laboratory. Curve A is for a nearly monoenergetic pion beam and has a sharp Bragg peak at a depth of 18 cm, curve B shows the depth-dose distribution when the peak is spread out to cover 10 cm using a dynamic range shifter. (Redrawn from: Raju *et al.*, 1979.)

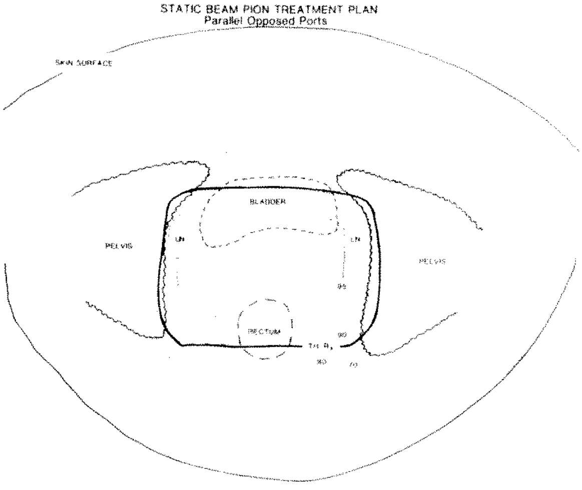


FIG. 6.

Isodose distribution obtained with parallel opposed beams of pions for the treatment of advanced carcinoma of the cervix (courtesy of Dr. Steven Bush).

the biological properties of the pions that is responsible (Kligerman *et al.*, 1974a, b). Figure 6 shows a typical treatment plan using pions to illustrate the superior dose localization that is possible with these heavy charged particles.

Los Alamos is the only pion facility at which a sizeable number of patients have been treated and at which controlled clinical trials have started, but TRIUMF (Tri-University Meson Facility) in Vancouver, Canada, and the PIOTRON in Zurich have been used to treat a few patients, and at the present time are a focus for research in the physics and radiobiology of negative pi mesons (Baarli *et al.*, 1976; Skarsgard *et al.*, 1977).

HIGH-ENERGY HEAVY IONS

An accelerator capable of generating a range of different high-energy heavy ions suitable for treating deep-seated human tumours is so complex, and its cost so high, that only one such machine is at present available in the world and this is located in Berkeley, California. However, in principle, if laboratory and clinical research leads to the choice of a single ion or a few ions as most suitable for radiotherapy, then a much simpler machine that would be adequate as a hospital-based dedicated source of heavy ions for medical use could be built at a fraction of the cost.

The unique facility presently available at the Lawrence Berkeley Laboratory is known as the BEVALAC, formed in 1974 by connecting the BEVATRON with the HILAC by means of a pipe 500 ft long, running down the hillside between the two machines. The HILAC had been used for many years to produce low-energy heavy ions with sufficient range to irradiate only monolayers of cells in culture. With the joining of the two machines, ions accelerated in the upgraded super HILAC pass down the connecting pipe and are accelerated further in the BEVATRON. In principle, the BEVALAC can accelerate ions of any Z, but to date efforts have focused on beams of nitrogen, oxygen, carbon, neon and argon, in sufficient intensities for radiobiological experiments.

A vast body of experimental data has been accumulated at the BEVALAC, comprising physical measurement of dose distributions and determination of radiobiological parameters using a variety of biological systems (Curtis *et al.*, 1978; 1979; Raju *et al.*, 1978; Blakely *et al.*, 1979). In addition, a limited number of cancer patients have been treated on an experimental basis. There are several beam configurations presently available at the BEVALAC, including high and low energy carbon and neon, plus a "low" energy argon beam. A higher energy argon beam is not considered to be useful because of the greater probability of the ions breaking up into smaller fragments as they pass through larger depths of absorbing material. Depth dose patterns for five of the available beam configurations are illustrated in Fig. 7. The depths at which the peaks occur are a function of the atomic number and energy of the particle concerned. The peak to plateau dose ratio is frequently in excess of five in unmodified Bragg peaks, but the Bragg peak is much too narrow to be utilized in the context of practical radiotherapy and it is necessary to spread out the Bragg peak to cover a tumour of realistic dimensions. This is accomplished by the use of a ridge filter, an absorber of

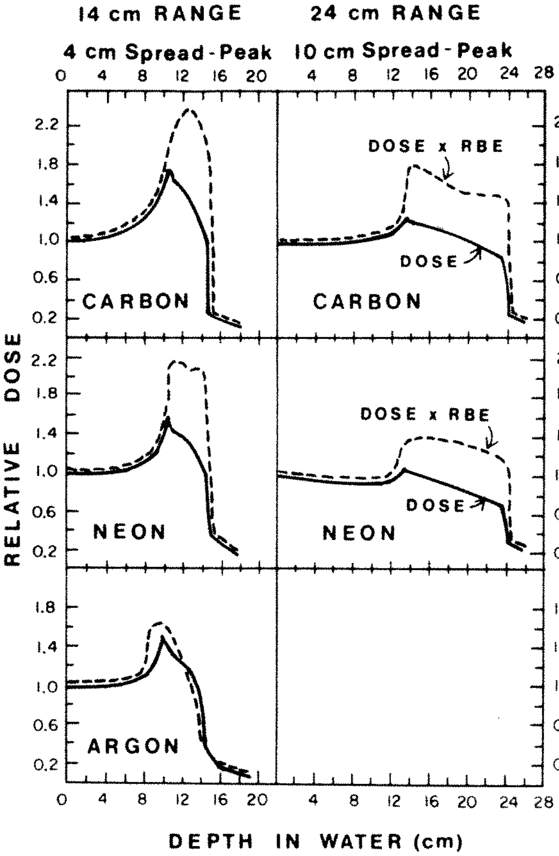


FIG. 7.

Depth-dose curves for the five beams available at the BEVALAC. In each case the full line shows the pattern of the physical dose with a ridge filter designed to spread the Bragg peak. The chain-line shows the distribution of the biologically effective dose—the product of dose and relative biological effectiveness (RBE). These lines must be regarded as illustrative only since RBE varies both with dose and tissue or cell type; the RBE values used to produce this figure were taken from the data for Chinese hamster cells by Blakely *et al.* (1979) corresponding to an X-day dose of about 2 Gy. (Redrawn from Blakely *et al.*, 1980.)

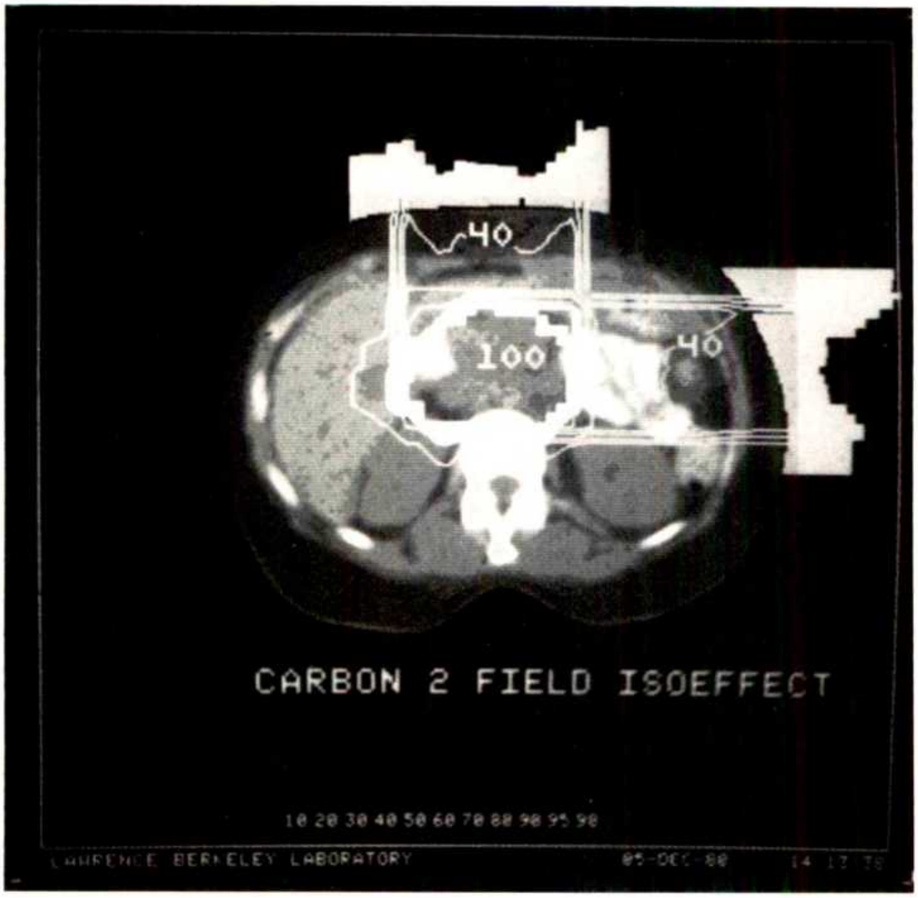


Fig. 8.

Treatment plan for a pancreatic tumour using two beams of carbon ions, shown as an overlay on a CT scan. Also shown are the external compensators to allow for both the contours of the patient and the tissue heterogeneity. The target volume is indicated by a thick white line and is enclosed by the 100% isodose line. The spinal cord and other critical normal tissues are spared to an extent that would not be possible with photons. (Courtesy of Drs. Castro and Chen, Lawrence Berkeley Laboratory, California.)

variable thickness that moves rapidly at right angles to the direction of the beam and causes the Bragg peak to "scan" a chosen range of depths. The spread-out Bragg peaks resulting from two such ridge filters, one 4 cm wide and one 10 cm wide, are shown in Fig. 7. The ridge filters are designed deliberately to produce a gradient of physical dose in the spread-out Bragg peak region, to allow for the fact that the biological effectiveness of the radiation varies through this region. The distal region of the spread-out peak contains a greater proportion of dose from Bragg-peak radiation compared to the proximal peak and therefore has a higher LET and greater biological effectiveness.

Radiobiological experiments have been performed with each of the five beams shown in Fig. 7 to determine the relative biological effectiveness (RBE) and the oxygen enhancement ratio (OER) of the radiation in various regions of the spread-out Bragg peaks. The results of the extensive investigations of Blakely *et al.* (1979) are summarized in Table II.

The dose pattern ultimately of interest is the "biologically effective" dose, defined to be the product of absorbed dose and RBE. This is shown as a dotted curve for each beam in Fig. 7. These curves illustrate that ridge filters can be designed to produce a relatively uniform biological effect over any region specified. These curves are no more than illustrative since RBE depends on the cell or tissue used for its determination and also on the dose level; the actual figures here refer to a particular cell line in culture and to a dose level of about 200 cGy(rad) of X rays.

TABLE II

OXYGEN GAIN FACTORS ($\text{OER}_X/\text{OER}_{HI}$)

	14 cm range 10 cm ridge filter	24 cm range 10 cm ridge filter
Carbon	1.3	1.1
Neon	1.3	1.2
Argon	2.2	—

It is evident from these data that a single beam of heavy ions results in a dose distribution vastly superior to that characteristic of a single beam of X rays in terms of uniformity and localization of the dose in the target volume relative to transit normal tissue. Of course, the use of two or three converging fields, with the spread-out Bragg peak regions coinciding, would further improve the localization of dose in the tumour volume. This is illustrated in Fig. 8 which shows an actual treatment plan used on the BEVALAC in which a pancreatic tumour was treated with two beams of carbon ions.

In terms of the biological properties of the radiation in the spread-out Bragg peak, it can be seen from Table II that either carbon or neon results in only a modest reduction in the dependence on oxygen. This is expressed in terms of an Oxygen Gain Factor, the ratio of the oxygen enhancement ratio for X rays divided by that for the high LET radiation. As a reference point, it is worth noting that this quantity is about 1.7 to 1.9 for neutrons; for carbon the comparable figure is 1.1 to 1.3 and for neon 1.2 to 1.3. Only in the case of argon is the Oxygen Gain Factor superior to that of neutrons. However, the range of the argon particles is limited because of fragmentation processes. In addition, the extra dose localization resulting from the elevated RBE in the spread-out peak region is less marked for argon because the LET in the Bragg peak is so high that RBE is actually falling due to the phenomenon of overkill. Filter design is clearly not optimized for the argon beam illustrated in Fig. 7.

COMPARING THE PARTICLES

Protons offer the unique opportunity to test the hypothesis that a further improvement in dose localization may lead to a concomitant improvement in the results of radiotherapy, without the added complication of any changes in biological properties. Protons do not differ significantly from X or γ rays in biological properties, they are relatively inexpensive compared with other heavy charged particles, and there is no dose-rate problem involved. Their role in the treatment of specialized tumours such as choroidal melanoma is already established; what remains to be tested is their wider role in broad beam radiotherapy.

Pions offer the dual advantages of an improvement in dose distribution as well as a modest contribution from the properties of high LET radiation. The sharpness of the dose distributions obtainable does not rival those of protons, largely because a substantial contribution to the dose comes from neutrons produced in the "stars". Because the Bragg peak has to be spread out over a distance required to encompass a tumour of realistic dimensions, the high LET component in the beam is diluted, and consequently the biological properties are intermediate between those of high and low LET radiation. Large and expensive accelerators are required to produce pions suitable for radiotherapy and even then the dose-rate that can be obtained is a limiting factor.

In principle, high-energy heavy ions offer the most flexible approach to combining the advantages of dose localization and the modification of biological properties. They all offer a sharp cut-off to the beam and a good increase in dose in the tumour volume compared with transit normal tissues. In order to produce a substantial modification of biological properties, including a reduction of the oxygen enhancement ratio that is comparable to neutrons, it is necessary to go to particles as heavy as argon. At the same time, this imposes a limit on the range of the particles that can be used because break-up and straggling occur for higher Z particles. It is fair to say that high-energy heavy ions are still very much in the experimental stage, and it has not yet been determined with any certainty what the optimal particles might be for radiotherapy. It seems quite clear at the present time that carbon ions, and possibly neon too, are of too low a Z inasmuch as while they offer obvious advantages of dose localization, their biological properties do not rival those of neutrons as far as the characteristics of high LET are concerned. Argon ions produce an oxygen gain factor superior to those of neutrons, but there are reasons to suppose that argon may be too heavy an ion, partly because of the break-up and straggling observed and partly because of the high entrance RBE and the fact that the LET of radiation in the pristine Bragg peak is so high that RBE begins to fall due to the over-kill effect. There are a number of possible contenders for a particle between neon and argon and a logical first choice for investigation would be silicon ions. Beams of this ion have been obtained at the BEVALAC, but to date no radiobiological data are available. A final judgment on the place and role of heavy ions, and their application to radiotherapy, should await a more complete set of data for particles of Z intermediate between neon and argon.

An attempt to compare the properties of the various ions, based on an idea by Raju, is presented in Fig. 9. On one axis is plotted the advantage of dose distribution and on the other the advantage of high LET. The evolution of conventional photon beams, from 250 kV X rays to ^{60}Co teletherapy units to megavoltage linear accelerators, has involved progressive improvements in the dose distribution with a negligible change in the LET of the beam. The trial of protons involves a further natural extension of this development inasmuch as the dose distribution advantage is further improved without any marked change in the LET of the radiation and without any of the advantages or disadvantages associated with high LET radiation. By contrast, the introduction of neutrons involves a substantial high LET advantage while the dose distributions that can be obtained are at best equal to those of ^{60}Co teletherapy units, and in many cases are intermediate between ^{60}Co and 250 kV X rays. Pions and high-energy heavy ions offer some advantage due to dose distribution as well as some advantage due to the high LET component of radiation in the beam. With a 10 cm spread-out Bragg peak, carbon and neon to different degrees are inferior to neutrons as far as high LET advantage is concerned, and it is necessary to go to argon or perhaps silicon before the heavy ions show any superiority over neutrons in the high LET advantage. In going to heavier and heavier ions the dose distribution advantage is gradually lost compared with protons.

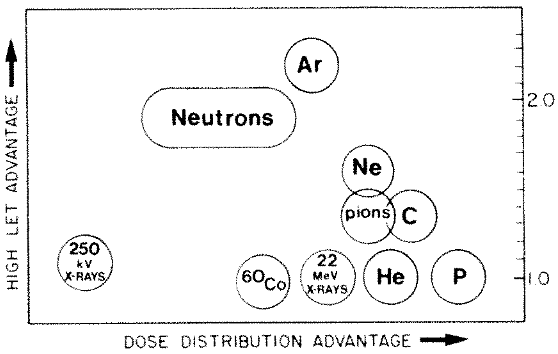


Fig. 9.

The particles compared. On one axis is plotted the advantage of dose distribution and on the other the benefits of high LET. Protons provide the best dose distributions available and high-energy argon ions the lowest oxygen effect in a practical situation. The other particles combine both advantages to various degrees. (Based on an idea by Dr. M. Raju.)

Conclusion

Heavy charged particles offer the possibility of impressive improvements in dose distribution and dose localization. Protons already have an established place for certain specialized applications. It remains to be demonstrated whether a wider application in radiation oncology, designed to exploit the dose distribution advantage, is worth the cost. It is also not clear whether a dose distribution advantage alone should be sought (protons) or whether the additional cost of adding the biological properties characteristic of high LET (pions, heavy ions) could be justified. This is an area of intense research activity and wide interest, but the answers to these questions are unlikely to emerge for several more years.

Acknowledgments

The author takes pleasure in acknowledging much useful discussion with Drs. Herman Suit, Joe Castro, Stan Curtis, Eleanor Blakely, Mortimer Kligerman and Steven Bush, who read the manuscript and made useful suggestions relating to their particular areas of interest.

REFERENCES

Baarli, J., Nordell, B. and Sullivan, A. H., 1976. Setting up of the π3 negative pion beam at SIN for radiobiological irradiations. *Atomkernenergie*, *27*, 175–176.

Blakely, E. A., Tobias, C. A., Ngo, F. and Curtis, S., 1980. Physical and radiobiological properties of heavy ions in relation to cancer therapy applications. In *LBL-11220: Biological and Medical Research with Accelerated Heavy Ions at the BEVALAC, 1977–1980.*

Blakely, E. A., Tobias, C. A., Yang, T. C. H., Smith, K. C. and Lyman, J. T., 1979. Inactivation of human kidney cells by high-energy monoenergetic heavy-ion beams. *Radiation Research*, *80*, 122–160.

Broerse, J. J., and Barendsen, G. W., 1973. Relative biological effectiveness of fast neutrons for effects on normal tissues. *Current Topics in Radiation Research*, *8*, 305–350.

Curtis, S. B., Tenforde, T. S., Parks, D., Schilling, W. A. and Lyman, J. T., 1978. Response of rat rhabdomyosarcoma to neon- and helium-ion irradiation. *Radiation Research*, *74*, 274–288.

Curtis, S. B., Tenforde, T. S. and Schilling, W. A., 1979. Review of the radiobiological response of a rhabdomysarcoma irradiated with heavy ion beams *in vivo* and *in vitro* results. In *High LET Radiations in Clinical Radiotherapy* (*European Journal of Cancer Supplement*). Ed. G. W. Barendsen, J. Broerse and K. Brew (Pergamon Press, Oxford), pp. 219.

Fowler, J. F., Morgan, R. L. and Wood, C. A. P., 1963. Pretherapeutic experiments with fast neutron beam from the Medical Research Council Cyclotron. I. The biological and physical advantages and problems of neutron therapy. *British Journal of Radiology*, *36*, 77–80.

Fowler, P. H. and Perkins, D. H., 1961. The possibility of therapeutic application of beams of negative π mesons. *Nature* (London), *189*, 524–528.

Gragoudas, E. S., Goitein, M., Koehler, A., Constable, I. J., Wagner, M. S., Verhey, L., Tepper, J., Suit, H. D., Brockhurst, R. J., Schneider, R. J. and Johnson, K. N., 1978. Proton irradiation of choroidal melanomas. *Archives of Ophthalmology*, *96*, 1583–1591.

Hall, E. J., 1969. Radiobiological measurements with 14 MeV neutrons. *British Journal of Radiology*, *42*, 805–813.

Hall, E. J. and Astor, M., 1979. The oxygen enhancement ratio for negative pi mesons. *International Journal of Radiation Oncology, Biology Physics*, *5*, 55–60.

Kligerman, M. M., Black, W. C. and Yuhas, C. A., 1977. Current status of clinical pion radiotherapy. *Radiology*, *125*, 489–492.

Kligerman, M. M., Von Essen, C. F., Khan, M. K., Smith, A. R., Sternhagen, C. J. and Sala, J. M., 1979a. Experience with pion radiotherapy. *Cancer*, *43*, 1043–1051.

Kligerman, M., Wilson, S., Sala, J., von Essen, C., Tsujii, H., Dembo, J. and Khan, M., 1979b. Results of clinical applications of negative pions at Los Alamos. In *High LET Radiations in Clinical Radiotherapy. European Journal of Cancer Supplement*. Eds. G. W. Barendsen, J. Broerse and K. Breur. (Pergamon Press, Oxford), pp. 61–66.

Raju, M. R., Amols, H. I., Bain, E., Carpenter, S. G., Cox, R. A. and Robertson, J. B., 1979. OER and RBE for negative pion beams of different peak widths. *British Journal of Radiology*, *52*, 494–498.

Raju, M. R., Bain, E., Carpenter, S. G., Cox, R. A. and Robertson, J. B., 1978. A heavy particle comparative study. II. Cell survival versus depth. *British Journal of Radiology*, *51*, 704–711.

Sinclair, W. K., 1968. Radiation survival in synchronous and asynchronous Chinese hamster cells *in vitro*. In *Biophysical Aspects of Radiation Quality*. Proceedings 2nd IAEA Panel, Vienna, 1967 (International Atomic Energy Agency, Vienna), pp. 39–54.

Skarsgard, L. D., Henkelman, R. M., Lam, K. Y., Harrison, R. W. and Palcic, B., 1977. Physical and radiobiological properties of the negative pi-meson beam at TRIUMF. In *Radiobiological Research and Radiotherapy*, November 22–26, 1976 (International Atomic Energy Agency, Vienna), Vol. II, pp. 87–100.

Suit, H. D., Goitein, M., Tepper, J., Verhey, L., Koehler, A., Gragoudas, E. and Schneider, R., 1977. Clinical experience and expectation with protons and heavy ions. *International Journal of Radiation Oncology, Biology, Physics*, *3*, 115–125.

Suit, H. D., Goitein, M., Munzenrider, J. E., Verhey, L., Gragoudas, E., Koehler, A. M., Urano, M., Shipley, W. U., Linggood, R. M., Friedberg, C. and Wagner, M., 1980. Clinical experience with proton beam therapy. *Journal of the Canadian Association of Radiologists*, *31*, 35–39.

Withers, H. R., Mason, K., Reid, B. O., Dubravsky, N., Barkley, H. T., Brown, B. W. and Smathers, J. B., 1974. Response of mouse intestine to neutrons and gamma rays in relation to dose fractionation and division cycle. *Cancer*, *34*, 39–47.

Yuhas, J. M., Li, A. P. and Kligerman, M. M., 1979. Present status of the proposed use of negative pi mesons in radiotherapy. *Advances in Radiation Biology*, *8*, 51–83.

Book review

Radiotherapy Treatment Planning. (*Medical Physics Handbooks* 7.) By R. F. Mould, pp. xii+204, 1981 (Adam Hilger Ltd., Bristol in collaboration with the Hospital Physicists' Association, London), £12·95.
ISBN 0-85274-504-4

The clarity of the layout of this handbook and of its more than 140 diagrams creates the immediate impression of a carefully prepared work. After an introduction and two short chapters on external beam therapy machines and radiation units (cgs and SI) the author deals at length with the single isodose curve. The various terms such as percentage depth dose, build up and back scatter factor are clearly defined and explained together with the factors upon which they depend. Wedge filters, tissue compensators and problems of beam obliquity and tissue inhomogeneity are also well illustrated and explained.

"The multiple field isodose curve pattern" is the heading for what is by far the longest section of the handbook where the emphasis is placed on the isodose patterns produced by differing arrangements of fields. Although I cannot easily accept the claim on the dust cover that this is a new approach it is certainly a helpful one. This section digresses from its main subject at different places to deal with patients' outlines and localization of the target volume, beam direction, immobilization of the patient and treatment simulators.

A chapter on electron beam therapy which deals very clearly with the differences between electron beams and photon beams for treatment of patients is followed by a chapter on the manual addition of isodose curves. Here the author quite rightly emphasizes that in spite of the widespread availability of computer planning systems the ability to do the job manually is still a prerequisite for certain examinations and that therefore the techniques involved need to be understood and mastered.

The final chapter on dose calculation methods deals with the determination of field doses and times and includes the use of TARs for fixed SAD and moving-field treatments.

There are many obvious and understandable problems in trying to deal adequately with this subject in a volume of limited size, and comments about the amount of detail given in the various sections will depend to some extent on the emphases and practices adopted in the experience of the individual critic, but I could not escape from a feeling of disappointment with this handbook. There really is an imbalance between theory and practice, the past and the present.

Simulators are highly expensive pieces of equipment which are considered by an increasing number of radiotherapists to be an indispensable aid to treatment planning yet they only merit a dozen lines of text.

The treatment plane in which a multiple-field isodose distribution is calculated is often not perpendicular to the top of the treatment couch. There are exact relationships between the angle of this plane to the horizontal, the planned beam angle and the angles of the gantry, couch and diaphragms which are set on an isocentrically mounted unit. An appreciation of these angular relationships is of more practical importance than the pin and arc which is no longer used in many centres where isocentric megavoltage machines are installed.

Although mantle treatments are mentioned there is no indication of the particular problem they introduce, that of determining the percentage depth dose and output for an irregular field.

The parameter most commonly used on a modern accelerator is not treatment time but "set dose" on an integrating dosemeter which can only indicate correctly for one chosen combination of field size and SSD.

In my experience these and similar problems encountered in the daily routine of a modern treatment department are the things which trouble registrars and radiographers and there is still a need for them to be discussed in a concise text for this group of people. Therefore, whilst I am pleased to recommend this handbook to any graduate entering the field of medical physics on the assumption that he can and should proceed to the reading of original papers on further points of detail, I feel that it will be of less value to registrars and radiographers. However, in spite of these deficiencies it should certainly be added to any comprehensive departmental library.

A. L. Bradshaw.

1981, *British Journal of Radiology*, 54, 782–786

Tolerance of brain to multiple courses of radiation therapy

I. Clinical experiences

By *A. Dritschilo, M.D.,

Georgetown Medical Center, Department of Radiation Medicine, Washington, DC

J. E. Bruckman, M.D.,

Division of Therapeutic Radiology, Mayo Clinic, Rochester, Minnesota

J. R. Cassady, M.D. and J. A. Belli, M.D.

Joint Center for Radiation Therapy, Harvard Medical School and Children's Hospital Medical Center, Boston, Massachusetts

(*Received August 1980 and in revised form February 1981*)

ABSTRACT

Patients with recurrent brain tumours years after initial radiation therapy pose a difficult management decision. Should retreatment be performed with irradiation, which carries a risk of necrosis, or should retreatment be with less effective agents but without unnecessary risks?

We present the results of retreatment of 32 patients at the Mayo Clinic and the Joint Center for Radiation Therapy. Clinical improvement was seen in all retreated patients. The median survival was 36 months after completion of the second course of irradiation. Eight patients (25%) were alive, free of disease, from 22 to 315 months after retreatment. Of the 11 patients alive at the time of analysis, eight were experiencing productive lives and three were suffering from severe neurological damage. Evidence of brain necrosis was observed in two patients (6%); however, only 10/21 patients underwent autopsy examinations. Reirradiation of patients with late recurrences of brain tumours may offer neurological improvement and prolonged survival without excessive risk of necrosis.

The role of radiation therapy in the retreatment of brain tumours is not well established. Factors such as the previous radiation dose, its fractionation, the overall time in which the dose was given, and the treated volume, are known to be important in the radiation tolerance of normal brain. In addition, the disease-free interval and possible recovery of radiation tolerance between courses of treatment may be considered in determining the potential ratio of risk to benefit in retreatment.

For the clinician contemplating reirradiation of a patient with recurrent brain tumour, few data are available on which to base a decision. One frequently relies on anecdotal personal experiences or the experiences of colleagues, and confidence in the final decision varies. Yet there are case reports in the literature of successful reirradiation; the patients had prolonged disease-free intervals with no apparent radiation-related complications (Kramer, 1969). In selected cases, retreatment with radiation provided effective palliation of symptoms and the risk of radiation injury was acceptable (Bouchard, 1958; Sheline, 1975).

For recurrent pituitary tumours, Sheline *et al.* (1964) compared the risks of radiation injury with the risks of tumour regrowth and found that retreatment risks were acceptable when their criteria for doses and disease-free intervals were met. In eight patients given second courses of radiation therapy, no evidence of brain damage developed for follow-up periods of three to 12 years (Sheline, 1971).

Recurrent brain tumours of other histological types have also been successfully retreated without overt necrosis. Bray *et al.* (1958) reported on retreatment of recurrent brainstem tumours in 12 children; improvement was observed in seven patients. Horns and Webber (1967) reported on a second treatment for recurrent symptoms in 12 patients with glioma; six had significant palliation lasting from eight to 29 months. In addition, there are several reports of retreatment with radiation and prolonged disease-free survival in patients with recurrent medulloblastoma (Penfield and Feindel, 1947; Paterson and Farr, 1953; Tice, 1962; Bloom *et al.*, 1969; Smith *et al.*, 1973; Harisiadis and Chang, 1977).

Current therapeutic interest in recurrent brain tumours is primarily concerned with chemotherapeutic regimens (Wilson, 1975; Duffner *et al.*, 1979). This attention is justifiable because of the poor overall prognosis for patients with recurrence. However, we believe that a subgroup of patients exists that may benefit from retreatment, since they do relatively well after reirradiation. In addition, the inclusion of such patients may bias results of uncontrolled trials.

---

*Address for reprints: A. Dritschilo, M.D., Georgetown Medical Center, Vincent T. Lombardi Cancer Research Center, Department of Radiation Medicine, 3800 Reservoir Road, NW, Washington DC 20007, USA.

There are no comprehensive reviews in the literature of the results achieved by reirradiation of patients with recurrent brain tumours.

We have reviewed the records of patients undergoing multiple courses of radiation therapy for brain tumours at the Mayo Clinic and at the Joint Center for Radiation Therapy. Our goal was to summarize the clinical experience in order to provide a basis for making decisions about reirradiation for this group of patients. There was a bias in the patient population, since most patients had recurrences after prolonged intervals. However, these patients are the ones who pose the most difficult management decisions and who are seen often enough to warrant a detailed review.

MATERIALS AND METHODS

The medical records of all patients undergoing two or more distinct courses of radiation therapy for brain tumours at the Mayo Clinic or at the Joint Center for Radiation Therapy were reviewed. The inclusive dates of the study were from 1950 to 1978 at the Mayo Clinic and from 1968 to 1978 at the Joint Center for Radiation Therapy. The clinical material reviewed consisted of patients treated for primary intracranial tumours with curative intent. Patients treated for brain metastasis due to primary tumours elsewhere were excluded.

The radiation therapy doses were estimated by review of the dosimetry data in the patients' records. These were frequently reported as mid-line doses. Doses for patients with pituitary tumours and gliomas treated at the Joint Center for Radiation Therapy were reported as minimum tumour doses, with a maximum dose not exceeding 15% of the minimum dose. In patients treated with 250 kV equipment, reported doses were corrected for the increased relative biological effectiveness to provide comparability with megavoltage-treated patients. Adequate follow-up data were available for all but one patient. Ten of 21 patients who died underwent autopsy. We accepted as evidence of necrosis either findings at autopsy in regions outside the tumour or, in patients who did not undergo autopsy, clinical evidence of neurological deficits not attributable to progressive tumours.

RESULTS

The series was composed of 32 patients, 21 from the Mayo Clinic and 11 from the Joint Center for Radiation Therapy. There were 18 males and 14 females, and 16 patients were 15 years old or younger. The radiation therapy details for each course of treatment are summarized in Table I. Patients were subdivided by histological types of tumours. Biopsy was not done in two patients; therapy was begun on the basis of clinical and radiographic findings.

Initial treatment of patients with medulloblastoma generally involved craniospinal irradiation. Subsequent courses excluded the spine. Patients with other histological types of tumours were treated with whole-brain (astrocytoma or glioma, grades III and IV) or subtotal brain irradiation. The records were generally accurate for purposes of determining regions of overlap of treatment fields. Estimations of volume of brain in the overlap regions, however, were not amenable to detailed analysis.

Twenty-one patients (64%) have died; ten underwent autopsy, and in one case the finding was compatible with necrosis. When first seen, one patient (No. 32) had leukoencephalopathy and negative results of brain scan and echography. He was classified as having had necrosis. This patient had also undergone chemotherapy with BCNU and vincristine for the eight months before death.

The median survival time for the entire group of patients was 36 months after completion of the second course of radiation therapy. Eight patients (25%) were alive without evidence of disease from 22 to 315 months after therapy. Three patients (9%) were alive with disease at 34, 105, and 219 months. The functional status of all patients was generally improved after irradiation; however, systematic grading was not possible retrospectively. In the 11 patients still living, neurological functional states were assessed (Table II). Three patients (Nos. 13, 14 and 28) appeared to be severely neurologically damaged. The others were experiencing productive lives.

DISCUSSION

There is a subgroup of patients with brain tumours who have late recurrences after initial management with radiation therapy. These patients present a therapeutic dilemma: which should be done—retreatment with irradiation, which has a risk of necrosis, or management without unnecessary risks, which is potentially less effective (Duffner *et al.*, 1979).

We addressed this issue by reviewing the records of patients given multiple courses of radiation therapy at the Mayo Clinic and the Joint Center for Radiation Therapy. Our observation was that these patients can be successfully treated with radiation therapy. They had good palliation, and in some cases long-term control of disease was achieved. Twenty-four percent survived more than five years after reirradiation. The risk of radiation necrosis was

TABLE I

SUMMARY OF RADIATION THERAPY COURSES BY HISTOLOGICAL TYPE OF TUMOUR

Patient	Age (years)	Sex	Initial surgery	Radiation treatment course	Dose, cGy (rad)	Fractions	Time (days)	Interval (months)	Follow-up status	Autopsy	Evidence of necrosis	Comments
Medulloblastoma												
1	4	F	R	1	5900*	23	23	20				15 month interval from second treatment
				2	1700*	16	16	6		+	—	
				3	1180*	12	12	7				
				4	2036*	16	16	2	DWD			
2	7	M	R	1	1888*	4	4	6				Massive dose, no histological evidence of necrosis
				2	1534*	6	6	6				
				3	1534*	4	4	5				
				4	5900*	12	13	16				
				5	4720*	10	10	2				
				6	3328*	11	11	22	DWD	+	—	
3	16	M	R	1	1180*	2	5	4				590 cGy fractions for the first 2 courses
				2	1180*	2	5	40				
				3	3102*	11	11	315	NED		—	Clinically well
4	24	M	R	1	4000	23	32	16				Autopsy at community hospital
				2	2600	15	16	30	DWD	+	—	
5	21	F	R	1	4550	22	24	67				
				2	3000	15	19	11	DWD	+	—	
6	5	M	R	1	5085*	24	46	32				Necrosis at autopsy
				2	2400	17	22	16				
				3	2400	12	15	12	DWD	+	+	
7	9	M	None	1	5180	28	50	13				
				2	2700	15	23	17	DWD	+	—	
8	9	M	R	1	4074*	23	42	171				
				2	3970	22	32	33	DWD	—	—	
9	8	M	R	1	4500	26	34	67				Mild retardation
				2	3750	20	28	36	NED		—	
10	8	M	R	1	4900	24	36	43				
				2	2900	15	22	24	DWD	—	—	
11	16	M	R	1	4300	22	35	46				
				2	2884	15	21	14	DWD	+	—	
Brainstem/thalamic glioma												
12	32	M	C	1	1554*	6	6	93				
				2	3717	21	25	27				
				3	3000	22	24	11	DWD	—	—	
13	8	M	None	1	4800	24	25	17				Left sided paresis, possible radiation damage
				2	2550	13	15	219	AWD		—	
Astrocytoma/glioma (grades I and II)												
14	12	F	R	1	5000	26	35	35				Dose not excessive
				2	2000	12	15	105	AWD		—	
15	26	M	C	1	2640	20	26	37				Dose not excessive
				2	3400	18	19	47	DWD	—	—	
16	17	F	C	1	3540*	20	25	91				Dose not excessive
				2	3000	20	26	143	NED		—	
17	4	M	R	1	4720*	20	28	172				Retarded
				2	3791	18	20	135	NED		—	
18	2	F	R	1	2900	15	29	39				Clinically well
				2	5000	27	46	22	NED		—	

Optic glioma												
19	20	F	R	1	4720*	29	40	148				
				2	4000	20	34	63	DWD	—	—	
20	3	F	R	1	2500	15	21	8				
				2	4900†	26	33	47	DWD	—	—	
21	1	M	R	1	3534*	17	25	38				Vision impaired
				2	4528	23	41	90	NED		—	
Astrocytoma/glioma (grades III and IV)												
22	37	M	R	1	4720*	23	29	21				Progression of tumour growth. Acute haemorrhage
				2	3338	17	21	14	DWD	+	—	
23	44	M	C	1	4602*	16	17	55				
				2	3000	19	22	33				
				3	2600	16	19	16	DWD	—	—	
24	59	F	R	1	3658*	15	18	16				
				2	1790	8	8	2				
				3	2055	10	11	15	DWD	+	—	
25	50	F	R	1	4634*	26	28	35				6 months interval is short to be certain about necrosis
				2	3872	23	32	6	DWD	—	—	
26	15	F	R	1	5950	31	45	53				6 month interval
				2	4350	23	39	6	DWD	—	—	
27	27	F	R	1	2382*	20	21	19				
				2	3260	26	31	14				
				3	3440	19	21	12	DWD	—	—	
Cystic astrocytoma												
28	5	M	R	1	4477*	21	26	12				Retarded
				2	4242*	19	21	300	NED		—	
Pinealoma												
29	22	F	C	1	4000	20	21	20				Limited area of brain irradiated. No radiation necrosis at autopsy
				2	3300	17	21	22	DWD	+	—	
Pituitary adenoma												
30	67	M	R	1	4000	20	29	93				Clinically well
				2	4000	20	28	34	AWD		—	
31	39	F	R	1	4500	20	22	63				Clinically well
				2	4000	20	21	83	NED		—	
Ependymoma												
32	7	F	R	1	4000	20	22	23				Clinical evidence of necrosis. Leukoencephalopathy
				2	2500	13	19	14				
				3	2500	14	15	32				
				4	2500	16	25	8	DWD	—	+	

R = Radical surgery with intent to remove tumour completely.
C = Conservative surgery with intent to decompress or biopsy only.
* = Orthovoltage equipment.
† = Dose to the overlapping region of the previous treatment field was 2900 cGy (rad).
DWD = Dead with disease.
NED = No evidence of disease.
AWD = Alive with disease.

TABLE II

Neurological and functional status of surviving patients

Patient	Age (years)	Interval (months)	Neurological status	Functional status
3	47	315	Blind since surgery	Lives with family. Full-time job
9	16	36	Mild retardation	Lives with family. Special School
13	27	219	Left-sided paresis. Ambulatory. Mass on CT scan (stable since 1977)	Lives at home. Part-time work. Became Eagle Scout
14	23	105	Retarded. Mass on CT scan (stable since 1976)	Lives in nursing home
16	37	143	Blind since diagnosis. Mild ataxia	Lives with family. Full-time job
17	29	135	Retarded	Lives with family. Part-time work
18	7	22	Intact	Lives with family. Attends school
21	12	90	Vision impaired	Lives with family. Attends school
28	30	300	Retarded. Left hemiparesis. Petit mal seizures	Lives in home for retarded
30	78	34	Visual field defect and decreased acuity. Mass on CT scan	No treatment-related impairment
31	46	83	Intact	Lives with family. Full-time job

increased; however, for most patients, the risks of tumour recurrence far outweighed this complication. In this series, only two patients had necrosis. Although late necrosis (years later) is still a risk for reirradiated patients, this is outweighed by the benefits of long-term tumour control.

Our current policy is to retreat selected patients with radiation therapy. Patients who have recurrence more than three years after the initial treatment are considered to have survived long enough to allow radiation tolerance to recover and to permit retreatment to essentially a full dose, 4000 to 5000 cGy (rad) (Dritschilo *et al.*, unpublished data). Treatment is instituted only if the patient has symptoms. The previous radiation therapy plans are reviewed and care is taken to avoid transit volumes in the new radiation beams. Treatment planning is important to minimize the volume of reirradiated brain.

With this approach, patients with slowly growing recurrent brain tumours may survive for a long time with neurological improvement without the risks of relatively ineffective chemotherapeutic agents. The risk of necrosis, although clearly there, is generally a late risk and is far outweighed by the risks of recurrent tumour.

REFERENCES

Bloom, H. J. G., Wallace, E. N. K. and Henk, J. M., 1969. The treatment and prognosis of medulloblastoma in children. A study of 82 verified cases. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 105*, 43–62.

Bouchard, J., 1958. Radiation therapy of malignant intracranial neplasms. *Progress in Radiation Therapy, 1*, 192–223.

Bray, P. F., Carter, S. and Taveras, J. M., 1958. Brainstem tumors in children. *Neurology, 8*, 1–7.

Duffner, P. K., Cohen, M. E., Thomas, P. R. M., Sinks, L. F. and Freeman, A. I., 1979. Combination chemotherapy in recurrent medulloblastoma. *Cancer, 43*, 41–45.

Harisiadis, L. and Chang, C. H., 1977. Medulloblastoma in children. A correlation between staging and results of treatment. *International Journal of Radiation Oncology, Biology, Physics, 2*, 833–841.

Horns, J. and Webber, M. M., 1967. Retreatment of brain tumors. *Radiology, 88*, 322–325.

Kramer, S., 1969. Radiation therapy in the management of brain tumors in children. *Annals of the New York Academy of Sciences, 159*, 571–584.

Paterson, E. and Farr, R. F., 1953. Cerebellar medulloblastoma. Treatment by irradiation of the whole central nervous system. *Acta Radiologica, 39*, 323–336.

Penfield, W. and Feindel, W., 1947. Medulloblastoma of the cerebellum, with survival for seventeen years. *Archives of Neurology and Psychiatry, 57*, 481–484.

Sheline, G. E., 1971. Untreated and recurrent chromophobe adenomas of the pituitary. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 112*, 768–773.

1975. Radiation therapy of recurrent gliomas. *Seminars in Oncology, 2*, 47.

Sheline, G. E., Boldrey, E. B. and Phillips, T. L., 1964. Chromophobe adenomas of the pituitary gland. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 92*, 160–173.

Smith, C. E., Long, D. M., Jones, T. K., Jr. and Levitt, S. H., 1973. Medulloblastoma. An analysis of time-dose relationships and recurrence patterns. *Cancer*, 32, 722–728.

Tice, G. M., 1962. Treatment and prognosis of medulloblastoma. *Journal of the American Medical Association, 182*, 629–631.

Wilson, C. B., 1975. Chemotherapy. Intact and recurrent tumors. *Seminars in Oncology, 2*, 73–74.

1981, *British Journal of Radiology*, 54, 787–798 SEPTEMBER 1981

Tolerance of the mature human central nervous system to photon irradiation

*D. R. Wigg, D.T.R., F.R.C.R., F.R.A.C.R., K. Koschel, Ph.D. and G. S. Hodgson, M.D.

Peter MacCallum Hospital, 481 Little Lonsdale Street, Melbourne 3000, Australia

(*Received February 1980 and in revised form May 1981*)

ABSTRACT

Tolerance of mature human brain to photon irradiation is described. Isoeffect curves have been derived for tolerance of large and small volumes of brain, by examination of doses determined empirically and in clinical use. These have been compared with isoeffect curves of thoracic myelitis, optic nerve and chiasm damage, and brain necrosis. The results show that the best-fitting Ellis-type equations, when five fractions per week are used, have low exponents for overall treatment time and high exponents for the number of increments (N), and are similar to published data on rat myelitis. Of the equations used to test the relationship between total dose and number of increments, the power curve was the best fit. Mean values of exponents for N derived for brain and spinal cord tolerance were 0.4 or more. These were similar to values obtained for optic nerve and chiasm damage, though the data are more limited for this complication. Brain necrosis is observed at slightly higher doses probably because of a difference in the end-point observed rather than because of any fundamental difference in tissue response. Evidence is presented to suggest that some repopulation may occur in widely spaced schedules. The use of the Ellis equation derived from connective-tissue data is inappropriate for central nervous system tissue, and its use may lead to a substantial risk of overdosage. A plea is made for adequate documentation of treatment details when human data are reported. The importance of dose per fraction is emphasized.

The relationship between total dose, number of fractions and overall treatment time for radiation damage to the mature human central nervous system has not been adequately established. A time–dose isoeffect curve of Strandqvist type for brain-stem with a slope of 0.22 was used by Boden (1950), and a slope of 0.26 was derived by Lindgren (1958) for brain. For spinal cord a value similar to Boden's was proposed by Pallis *et al.* (1961) and 0.28 was suggested by Maier *et al.* (1969). These values were supported by Vaeth (1965), Jellinger and Sturm (1971), and Palmer (1972). However, to include apparent inconsistencies it has been necessary either to lower Boden's suggested dose levels or postulate tissue idiosyncrasies.

Overall treatment time is important in time–dose fractionation formulae for tissues having considerable capacity for rapid repair of sublethal injury or repopulation during a course of radiotherapy. This is reflected in the Ellis (1969) equation for connective tissue in which the exponent for overall treatment time (T) is 0.11. Such a relationship does not necessarily apply to tissues with limited capacity for repopulation or a different capacity for repair. Negligible exponents for T have been shown for rat spinal cord, and these were maintained for intervals up to eight weeks between schedules (van der Kogel *et al.*, 1976; van der Kogel, 1977b).

Much of the uncertainty regarding isoeffect curves for human brain has resulted from studying time–dose relationships, rather than total dose versus number of fractions (N).

In this paper, the tolerance of mature human brain to photon irradiation is examined by deriving isoeffect curves for fractionated regimes in common use, and comparing these with the effects of excessive dose resulting in brain necrosis, thoracic myelitis, and optic nerve and chiasm damage.

When adequate data are available for treatment regimes using five fractions per week, the exponents for N and T were found to be similar to those described by van der Kogel *et al.* (1976) for rat myelitis. When total dose versus number of fractions was examined, the exponent of N for brain and spinal cord was 0.4 or more.

Consequently, the biological effect is more dependent on dose per fraction in the regions of the central nervous system examined than it is in normal connective tissue. The importance of dose per fraction is stressed.

MATERIAL AND METHODS

Isoeffect curves and formulae have been developed from empirically determined doses in clinical use for large and small volumes of brain. The data used have been derived from many centres and cover a spectrum of treatment regimes as wide as could be obtained. These are compared with isoeffect formulae derived from published data describing the complications following excessive doses which have resulted in radiation myelitis of the thoracic cord, optic nerve or chiasm damage, or brain necrosis.

---

*Present address: Radiotherapy Department, Royal Adelaide Hospital, North Terrace, Adelaide 5000, South Australia.

All data sets were subjected to the same sequence of analysis, consisting of fitting data to a straight line, exponential curve, power curve, hyperbola and inverse hyperbola, by data transformation and linearization. Coefficients of the relevant equations with their 95% confidence and 95% prediction limits were determined for each curve-fitting procedure. All data were also fitted by a conjugate gradient search procedure (Powell, 1965) to the Ellis-type formula, total dose$=KN^aT^b$.

The sources of the data used are discussed in the individual sections. Much of the published data could not be used because of lack of treatment details, particularly regarding the number of increments used. Doses quoted in röntgens have been converted to cGy (rad), and bone corrections (Johns and Cunningham, 1969) have been made as indicated in the appropriate Tables. RBE corrections have also been made for orthovoltage and electron data (Paterson, 1960). Barotherapy data have been excluded, as have data where dose per increment has varied.

The data points analysed for the series of brain necrosis, thoracic myelitis, and optic nerve and chiasm damage have been selected to include only "threshold" doses. These are the minimum total doses for a treatment regime for a given number of increments (N) at which the complication occurred. The approach is similar to that of Friedman and Pearlman (1955) who used the technique of minimum corroborated tumour lethal dose to minimize distortion of isoeffect curves of tumour control by excessive doses. Isoeffect curves have also been derived for subsets of thoracic myelitis, optic nerve and chiasm damage where a range of incidence of these complications is stated or can be estimated. This results in a narrowing of the confidence limits and is particularly useful to examine the "threshold" isoeffect curves. There was insufficient data for brain necrosis to determine complication rates.

RESULTS

Brain tolerance derived empirically

Published empirically-determined tolerance doses for whole brain and large and small volumes of brain are listed in Table I. To these are added dose-time-fractionation schedules in use at the centres visited by one of the authors (D.R.W.), which are listed in the appendix. Most regimes were given at five frac-fractions per week, or with only minor departures from this, as is indicated in the Table.

Regression analyses of the data for whole brain or large volume of brain, either separately or combined, show that a straight line ($TD=a+bN$) fitted as well as the power curve equation, $TD=aN^b$. This was also the case for the data on small volumes but with different fitting constants.

Between 1934 and 1952, 84 cases of brain tumour were treated by a hyperfractionation regime adopted by R. Kaye Scott, consisting of three or four schedules with intervals, usually of three, six and then nine months, between schedules. Similar techniques have been reported by Kaplan (1941) and

TABLE I

Tolerance doses of mature human brain derived empirically. Dose per increment constant, five or more increments per week

	Total dose cGy (rad) (TD)	Number of increments (N)	Overall treatment time, days (T)
Whole brain			
Salazar *et al.* (1976)	6000	33	46
Kramer and Lee (1974)	5000	25	35
Marsa *et al.* (1975)	4000	20	28
Todd (1965)	3750	15	21
Visited centres	6000	35	49
Visited centres	6000	35	49
Visited centres	6000	33	46
Visited centres	6000	30	42
Visited centres	5000	27	37
Visited centres	5000	25	35
Visited centres	5000	25	35
Visited centres	4000	20	28
Visited centres	3000	10	14
Large volume of brain			
Bouchard (1966)	6500	38	54
Lindgren (1958)	4916†	24	30
Todd (1965)	4000	15	21
Boden (1950)	3441†*	15	17
Visited centres	6000	34	48
Visited centres	5500	30	42
Visited centres	5500	28	38
Visited centres	5250	25	35
Visited centres	5000	25	35
Visited centres	4500	20	28
Visited centres	3000	8	12
Small volume of brain (approximately 1/3 or less)			
Kramer and Lee (1974)	6500	35	49
Todd (1965)	4500	15	21
Boden (1950)	4425†*	15	17
Visited centres	6000	30	42
Visited centres	5500	25	35
Visited centres	5000	20	28
Visited centres	4250	15	21

*Bone corection 10%.

†Not strictly five increments per week.

In all tables the doses have been converted (where necessary) to ^{60}Co γ rays or megavoltage X rays.

Jenkinson and Oldberg (1941), but these lacked treatment details. The dose per increment usually varied between schedules. A common regime was to start at 150 cGy (rad) per increment for the first schedule, reducing to 125 cGy (rad) for the second and further reductions for subsequent schedules. All fields were treated daily. No cases of brain necrosis were known to have occurred (Kaye Scott, 1978) and a retrospective review of all the records revealed no evidence of this complication. Table II shows 17 of the 84 cases who survived 4.8 years or more. After this time interval necrosis is unlikely to occur (Kramer and Lee, 1974). Five cases had a constant dose per fraction throughout the regime. Most of these long survivors had cystic gliomas or brain-stem gliomas.

The mean tendency of the power curve derived from the combined data for whole brain and large volumes was,

$$TD=(862\pm156)N^{(0.55\pm0.06)} \quad . \quad . \quad (1)$$

where TD=the total dose in cGy (rad);
N=the number of increments.

For small volumes of brain the mean tendency of the power curve derived was,

$$TD=(1273\pm221)N^{(0.46\pm0.06)} \quad . \quad . \quad (2)$$

Figure 1 shows these two power curves with their 95% confidence limits and extrapolated mean values. The cases listed in Table II were plotted but were not used in deriving the above equations. The time–dose-fractionation equation derived from combined data for whole and large volumes of brain was

$$TD=(860\pm337)N^{(0.46\pm0.20)}T^{(0.09\pm0.20)} \quad (3)$$

For small volumes of brain, the values were

$$TD=(1269\pm102)N^{(0.41\pm0.02)}T^{(0.04\pm0.004)} \quad (4)$$

Thoracic myelitis

Adequately documented cases of permanent thoracic myelitis are listed in Table III. Only "threshold" total doses given at a constant dose per

TABLE II

Tolerance of mature human brain, hyperfractionation series. Bone and RBE corrections made. Duration of regime includes intervals between schedules, figures in brackets exclude these intervals

Total central dose cGy (rad)	Number of increments (N)	Duration of regime (days)	Survival (years)
Large volume of brain			
13110	100	810	13
11012	94	410	21
12718	90	2640	19
9440	88	480	7.5
9960	87	600	4.8
9460	83	540	18
11316	81	840	28
9963	80	540	8
8916	71	450	13
7341	70	480	23
12674*	87	420 (108)	9
10608*	87	690 (122)	4.8
8460*	60	630 (90)	26
7925*	49	890 (108)	23
Small volume of brain			
9964	80	510	5.6
9079	78	1050	15
14867*	81	1018 (128)	9.8

*Dose per increment remained constant.

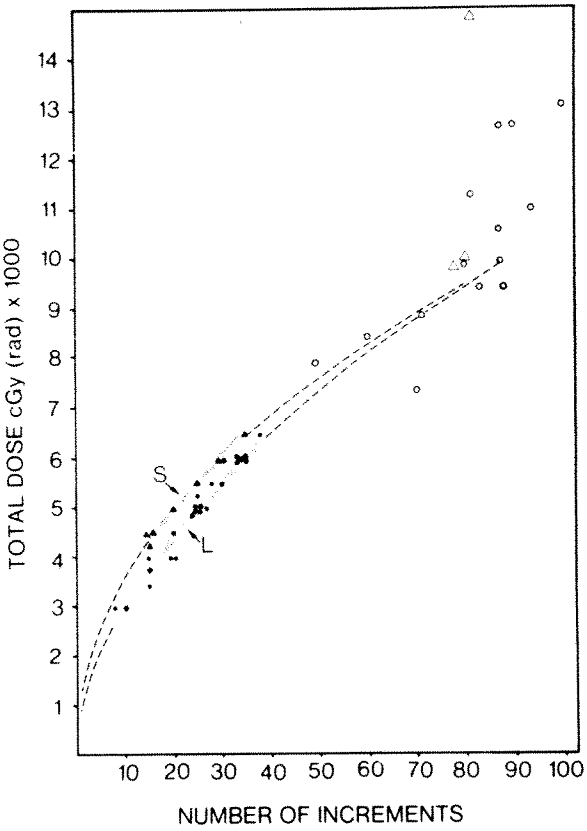


Fig. 1.

Isoeffect curves for tolerance of mature human brain derived from empirically determined data. L, whole brain and large volume data (●). S, small volume data (▲). Hatched area encloses the 95% confidence limits. Interrupted lines, extrapolated mean values. Open figures from hyperfraction series, ○ large volume, △ small volume.

TABLE III

RADIATION MYELITIS OF THORACIC CORD

	Total dose cGy (rad) (*TD*)	Number of increments (*N*)	Overall treatment time (days) (*T*)	Length of cord (cm)	Estimated incidence %	Series
Reinhold *et al.* (1976)	6515	30†‡	43	15	44	B
^{60}Co or MV X rays	6282	29†‡	44	12.5	25–44	B
^{60}Co or MV X rays	6912	28†	42	11	> 50	C
^{60}Co or MV X rsys	6174	27†‡	37	10.5	44	B
^{60}Co or MV X rays	5342	26†‡	37	17	25	A
^{60}Co or MV X rays	6186	25†	35	13	44–50	B
^{60}Co or MV X rays	6161	24†	33	10	50	B
^{60}Co or MV X rays	6727	23	64	11	50–100	C
^{60}Co or MV X rays	6953	22	55	14	100	C
^{60}Co or MV X rays	5609	20†	26	10	50	B
^{60}Co or MV X rays	5782	19	48	9	50	B
^{60}Co or MV X rays	6354	18	42	9.5	100	C
Atkins and Tretter (1966)	3987	12	26	21	19	A
	3651	10	21	9	19	A
22.5 MeV electrons	1993	2	7	10–29	31	B
Locksmith and Powers (1968)	4145	16†‡	21	14	12.5	A
22.5 MeV electrons	4061	15†‡	21	21	12.5	A
Wara *et al.* (1975)	6700	37†‡	55	?	35	B
^{60}Co or MV X rays	6753	36†‡	55	?	35	B
^{60}Co or MV X rays	3300	6	23	?	40	B
Coy *et al.* (1969) ^{60}Co	4200	8	29	11	55	C
Smithers *et al.* (1943)	5765	31†	39	15	2.5	A
HVL 3.7 mm Cu						
Atkins and Tretter (1966)	4985	25	35		0	0
	3987	20	28		0	0
Boden (1950)	3441*	15	17		0	0
Wara *et al.* (1975)	3000	10	?		0	0
Wara *et al.* (1975)	2000	5	?		0	0

*Bone correction 10%.
†Five increments per week approximately.
‡Five increments per week and 12.5%–44% incidence.
Series used for TDF (equation (7)).

fraction are included. RBE corrections were made for orthovoltage and electron cases, and bone corrections were made for orthovoltage cases. The series contains some cases which departed from five fractions per week.

Cases with similar incidences of myelitis were grouped for analysis to narrow the confidence limits of the isoeffect curves derived. Cases have been eliminated where this information was not available or could not be derived reasonably accurately. The incidence of myelitis was stated (Locksmith and Powers, 1968; Atkins and Tretter, 1966), or can be derived from the text (Smithers *et al.*, 1943; Wara *et al.*, 1975). The incidence for the Reinhold *et al.* (1976) series has been estimated by calculating the equivalent dose (ED) (Wara *et al.*, 1975) for each of this series with and without myelitis. Groups with similar ED values, with and without myelitis, can be compared and the incidence derived.

Estimates of the average latent period for the onset of myelitis vary from nine months (van den Brenk *et al.*, 1968) to 17 months (Palmer, 1972). The observed period in this series exceeded one year, with the exception of Coy *et al.*'s (1969) observations which were made at nine months. The probable incidence for the latter has therefore been calculated from its ED value.

Three groups have been examined separately. The probable incidences of myelitis within these groups are respectively 2.5–25% (A series), 25–50% (B series), > 50% (C series). A further subset with 0% risk represents doses reported by the authors quoted in Table III to carry no risk of myelitis.

The *N* values for the B series, 2 to 37, encompassed those for the A and C series. The mean tendencies for both the B series and the A, B and C series combined were almost identical. For the B series the values were:

$$TD = (1530 \pm 155) N^{(0.43 \pm 0.03)} \quad . \quad . \quad (5)$$

The dose-fractionation regimes at which the probability of myelitis occurring is very low and approaches

0% ("threshold" of tolerance) are difficult to define with accuracy because of data limitations. Guidelines available (Fig. 2) include the lower 95% confidence limits of series A, and the mean tendency of 0% series. An alternative was to derive the *a* and *b* values at zero incidence (a_0 and b_0) by extrapolation of the mean *a* and the mean *b* values of the individual incidences within each of the three series A, B and C. The mean tendency for "threshold" of tolerance using the a_0 and b_0 values derived was

$$TD = 1309N^{0.41} \quad . \quad . \quad . \quad . \quad (6)$$

Examples of "threshold" doses derived from equation (6) are given in Table III and plotted in Fig. 2. This figure shows that the TD values obtained are very similar to the 95% confidence limits of the A series, which however lacks data below ten fractions. As these values are similar to the 95% prediction limits of the A, B and C series combined (between 140 and 220 cGy (rad) higher) the latter have not been included in Fig. 2.

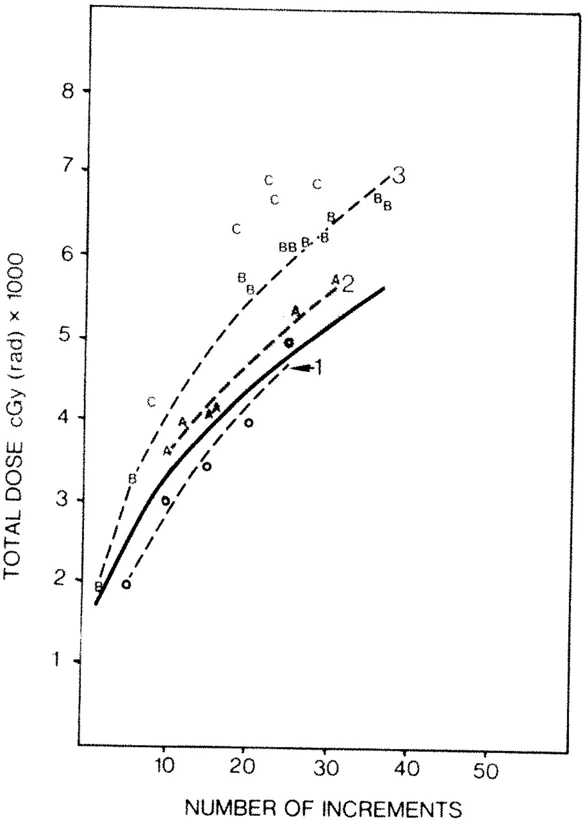


Fig. 2.

Isoeffect curves for thoracic myelitis. 1, mean tendency 0% incidence (0). 2, mean tendency 2.5% to 25% incidence (A), with 95% confidence limits hatched. 3, mean tendency A, B and C series combined, which is almost identical to mean tendency of 25% to 50% incidence (B). Continuous line, threshold of tolerance (equation (6)).

One series (Table III) treated with five fractions per week, with an incidence between 12.5% and 44%, was available to derive a time–dose-fractionation equation. As the lowest number of fractions was 15 (*N* from 15 to 37), and as only eight cases were available, extrapolation below 15 fractions becomes increasingly unreliable. The values derived were:

$$TD = (796 \pm 147)N^{(0.54 \pm 0.05)}T^{(0.05 \pm 0.01)} \ . \quad (7)$$

Optic nerve and chiasm damage

There are far fewer case reports of this complication than of thoracic myelitis, and again many exclusions were necessary due to inadequate documentation of treatment details. The number of increments was not reported by Ross *et al.* (1973), Rosengren (1958), Crompton and Layton (1961), Buys and Kerns (1957), Ellis (1949), or Spillane (1951). The total dose was not clearly stated by Martins *et al.* (1977) or Marsa *et al.* (1975), and cases reported by Orth (1973) and Ghatak and White (1969) are excluded because of uncertainty of the incidence, and cases with lower dose per increment are available. Cases treated with continuous irradiation (Hartog *et al.*, 1965; Forrest *et al.*, 1956), and those treated with particle irradiation by Linfoot *et al.* (1971) and Kjelberg and Kliman (1973), are also excluded because of uncertainties of the RBE values and details of dose distribution. One case treated with a grossly excessive dose of 8×1000 cGy (rad) (Urdaneta *et al.*, 1976) has been excluded.

The number of increments in Schukovsky and Fletcher's series (1972) can be derived from the NSD values quoted. Two of 15 cases developed central retinal artery thrombosis nine and 15 months after treatment. The observed period was five years and the incidence was estimated to be 13%. Three of 15 cases developed optic nerve blindness between four and five years after treatment and the incidence was estimated as ⩾20%. Harris and Levine (1976) reported five cases of damage to optic pathways; the incidence can be derived from the text. Aristizabal and Caldwell (1976) reported four cases of blindness and one case of brain necrosis. The brain necrosis case could not be identified but it is unlikely to alter the percentage complication rate appreciably. The doses used in this series are the means of the range of doses quoted. Schatz *et al.* (1975) reported three cases, two of which had dissimilar doses and are included. Two of these cases developed visual field defects identical to so-called patterns of ischaemic optic nerve and chiasm disease. The authors considered that the doses used were in a range at which this complication is particularly uncommon and these cases have therefore been included in the series of >0 $<20\%$ incidence.

Table IV shows the details of the cases examined. The power curves have been plotted in Fig. 3, although the straight line fitted as well, reflecting the small range of N available.

When all cases with a minimum dose per fraction were combined, the exponent for N was 0.59. This high value resulted from inclusion of several high-dose, high-incidence cases. When only those cases with a more uniform incidence of >0 $<20\%$ are considered,

$$TD=(1815\pm1590)N^{(0.33\pm0.25)} \quad . \quad . \quad (8)$$

Within the limits of the data available, the best guides to the "threshold" of tolerance are the lower 95% confidence limits of the series with >0 $<20\%$ incidence, and the zero incidence line derived from doses suggested as being safe by the authors listed in Table IV. The lower 95% confidence limits do not include all data values and are therefore slightly too high. TD values for threshold of tolerance for thoracic myelitis defined by equation (6) are within 40 to 70 cGy (rad) above the zero incidence line, and 60 to 190 cGy (rad) below the 95% confidence limit for optic nerve and chiasm damage. This isoeffect curve would appear to serve equally well for both thoracic myelitis and optic nerve and chiasm damage, when N lies between 16 and 28.

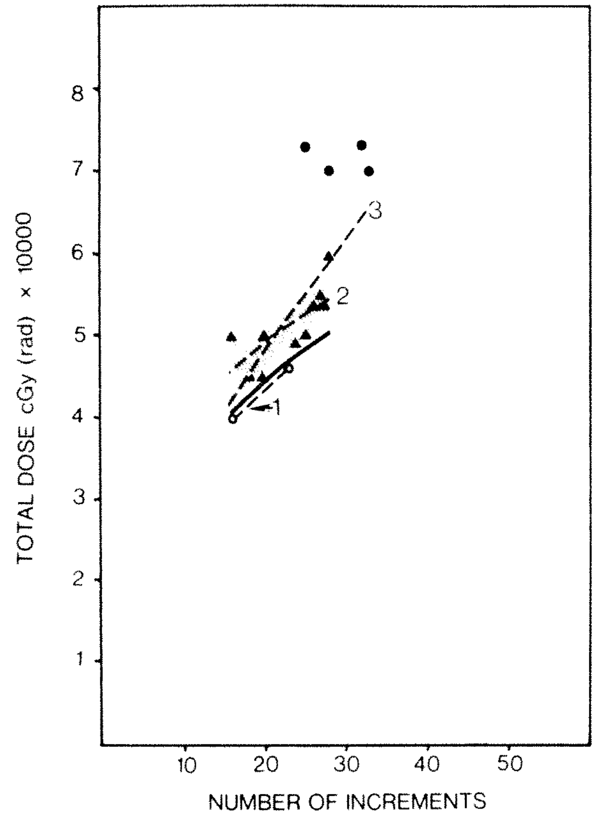


Fig. 3.

Isoeffect curves for optic nerve and chiasm damage: 1, isoeffect line for 0% incidence (0). 2, mean tendency $>0\%$ $<20\%$ incidence (▲), with 95% confidence limits hatched. 3, mean tendency of all cases combined. Incidence $\geq 20\%$ (●). Continuous line, threshold of tolerance from myelitis data (equation (6)).

Four cases were reported as having a thrombotic or microvascular basis for the observed effect. No difference between dose-fractionation relationships for these and the remaining cases could be detected. This is in contrast to the occurrence of central retinal artery thrombosis occurring at lower doses than optic nerve blindness, as reported by Schukovsky and Fletcher (1972). However, the numbers are too small to draw firm conclusions.

The time–dose-fractionation equation derived for the >0 $<20\%$ incidence cases treated with five fractions per week was:

$$TD=(1744\pm626)N^{(0.34\pm0.12)}T^{(0.000\,006\pm0.004)} \quad (9)$$

Brain necrosis

There are few adequately documented cases of brain necrosis suitable for examination. Many exclusions were necessary because of uncertainties of dose, *e.g.* Scholz and Hsu (1938) and Foltz *et al.* (1953); and uncertainties of the number of fractions used, *e.g.* Lampert and Davis (1964), Malamud *et al.* (1954), Crompton and Layton (1961) and O'Connell and Brunschwig (1937). Because of possible intolerance of the hypothalamic region (Arnold *et al.*, 1954), cases of necrosis in this region reported by Kramer *et al.* (1968), Almquist *et al.* (1964) and Peck and McGovern (1966) have been excluded. Also excluded are cases treated with multiple widely-spaced schedules. The remaining suitable cases are listed in Table V.

All were treated with orthovoltage beams. Bone and RBE corrections have therefore been made. The smallest volume in the series was treated with a 5 cm diameter beam.

Pennybacker and Russell (1948) reported five cases, but only case 1 was suitably documented and treated with a single schedule. The dose has been recalculated at a depth of 1.5 cm. Only Boden's (1950) cases 1, 4 and 6 were included; the remainder were excluded because of treatment with multiple

TABLE IV

RADIATION DAMAGE TO OPTIC NERVE AND CHIASM

	Total dose cGy (rad) (*TD*)	Number of increments (*N*)	Overall treatment time (days) (*T*)	Estimated incidence %
Schukovsky and Fletcher (1972)	7300	32	43	$\geqslant 20$
MV X rays or ^{60}Co	7300	25	34	$\geqslant 20$
MV X rays or ^{60}Co	7000	33	43	$\geqslant 20$
MV X rays or ^{60}Co	6000†	28*	40	13
MV X rays or ^{60}Co	5500†	27	34	13
Harris and Levine (1976)	4500	20	32	9.6
MV X rays	7000	28*	45	100
MV X rays	5000	20	29	8.3
MV X rays	4500	18	26	9.6
Aristizabal and Caldwell (1976)	4900	24	34	< 10
MV X rays or ^{60}Co	5400	27	38	< 20
Schatz *et al.* (1975)	5000†	25	36	< 20
^{60}Co	5400†	27	36	< 20
Visited centres	5000	16	21	12
Harris and Levine (1976)	4000	16	23	0
Aristizabal and Caldwell (1976)	4000	23	30	0

All cases treated with five increments per week except *.
†Vascular aetiology.

TABLE V

BRAIN NECROSIS

	Case number	Per cent bone bone correction	Total dose cGy (rad) (*TD*)	Number of increments (*N*)	Overall treatment time (days) (*T*)	Estimated incidence %
Pennybacker *et al.* (1948)	1	10	1991	1	1	?
Boden (1950)	1	10	5948*	15‡	17	24–53
Boden (1950)	4	10	5359*	15‡	17	24–53
Boden (1950)	6	10	5457*	15‡	17	29
Dugger *et al.* (1954)		10	4181*†	10‡	10	?
Wachowski and Chenault (1945)	1	5	8053†	57	105§	?
	3	10	8662†	49	87§	?
Lindgren (1958)	171	10	7128	21‡	27	?38
Lindgren (1958)	188	10	7374	24‡	31	?38
Lindgren (1958)	301	10	7078	27	70§	?38
Lindgren (1958)	116	10	8062	27	70§	?38
Lindgren (1958)	27	10	7964	28	78§	?38
Lindgren (1958)	158	10	7128*	30‡	38	?38
Lindgren (1958)	135	10	9930	31	70§	?38
Lindgren (1958)	41	10	7177†	35	88§	?38
Lindgren (1958)	192	10	8259	38	67§	?38
Lindgren (1958)	203	10	7079†	42	90§	?38
Boden (1950) (large volume)		10	3441	15	17	0
Lindgren (1958)		10	5899	35	88	0
Lindgren (1958)		10	4917	24	30	0
Lampert (1959)		0	4911	20	29	Demyelination

*ED values 1536–1818 ret, treated at five increments per week.
†ED value < 1541 ret (1332–1541).
‡Five increments per week approximately.
§Split or interrupted course.

schedules or else because necrosis occurred only in the medulla. The dose used by Dugger *et al.* (1954) has been recalculated at 2 cm assuming a beam of HVL 0.5 mm Cu. Case 2 of Wachowski and Chenault (1945) had multiple treatments and was excluded; and treatment of cases 1 and 3 was interrupted, extending the overall treatment time. Lindgren (1958) reported 16 cases of necrosis; of those excluded, three were children, one had probable superadded infection, and two had multiple treatments. Included are seven cases who had split course regimes with six to eight weeks between schedules.

There are no reliable data for the incidence of necrosis at the dose–time-fractionation regimes used. In Boden's middle-ear series, 17 cases survived one year or more for assessment. Four developed necrosis, and five others developed progressive paralysis presumed to be radiation effects, giving an incidence between 24% and 53%. Lindgren's (1958) cases were treated by a fairly uniform technique; of these, 21 died after one year or more and were examined at autopsy; 38% had evidence of necrosis. Uncertainties regarding the assumed random selection of cases for autopsy and some variation in dose preclude assessment of the true incidence.

When all "threshold" cases were combined (Table V, excluding Boden's cases 1 and 6 and Lindgren's case 116), N ranges from 1 to 57 and the best fitting equation was

$$TD=(2009\pm 510)N^{(0.38\pm 0.08)} \quad . \quad (10)$$

The lower 95% prediction limit of this series is shown in Fig. 4.

Table V includes a subset of 0% risk representing doses recommended as being "safe" by the authors quoted. It includes one regime reported by Lampert *et al.* (1959) which caused gross demyelination, with small areas of central necrosis seen on microscopic examination. This case probably represents the borderline of gross necrosis and has been included with the 0% incidence series.

In the absence of reliable incidence data, an attempt to group cases with likely similar probabilities of complication has been made by grouping according to similar ED values. The best fitting equation for cases with ED values less than 1541 ret was

$$TD=(1665\pm 959)N^{(0.40\pm 0.15)} \quad . \quad (11)$$

Figure 4 shows the 95% confidence limits of this series (equation (11)). Examples of the lower limit are listed in Table VI as a guide to the "threshold" of tolerance of brain necrosis. An alternative more conservative estimate of "threshold" values is given by the lower 95% prediction limits for all cases combined (equation (10)), but because of data limitations these may be too conservative especially within the higher range of N values.

Only one small series treated at five fractions per week (ED values of 1536 to 1818 ret) was available for derivation of a time–dose-fractionation equation. The values were

$$TD(1984\pm 34)N^{(0.40\pm 0.008)}\,T^{(0.000\,06\pm 0.009)} \qquad (12)$$

Discussion

The exponents for N of 0.55 for tolerance of large volumes of brain (equation (1)) and 0.46 for small

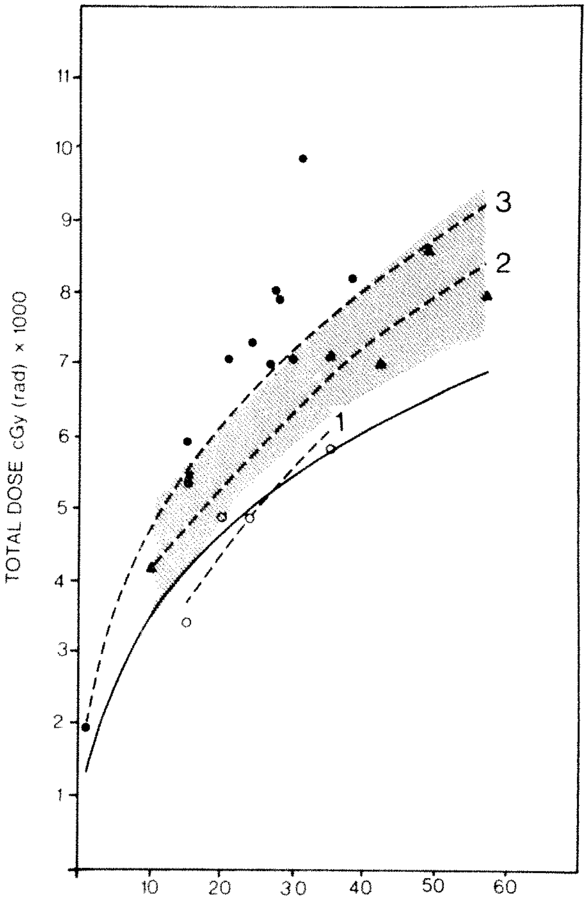


Fig. 4.

Isoeffect curves for brain necrosis. 1, mean tendency 0% incidence (0). 2, mean tendency for cases with ED values < 1541 ret (▲) (equation (11)), with 95% confidence limits hatched. 3, mean tendency all "threshold" cases combined (equation (10)), with the lower 95% prediction limits of this series shown as a continuous line.

volumes (equation (2)) are slightly higher than those for thoracic myelitis and brain necrosis when data are available which encompass a wide range of increments. Thus, for the series including all myelitis cases combined and the B series myelitis (equation (5)), the exponent was 0.43. This is similar to the value for rat myelitis of 0.40, derived by White and Hornsey (1978) for one to 30 fractions, 0.44 for one to four fractions (Masuda *et al.*, 1977), and 0.42 for one to 20 fractions (van der Kogel, 1977a). There are insufficient human data to confirm whether a constant slope is maintained when small numbers of increments are used, as occurs with rat myelitis but not with radiation pneumonitis of mice (Field *et al.*, 1976). The exponent for brain necrosis, when a wide range of increments is available, is 0.38 (equation (10)) and is also slightly lower than the empirically determined values for brain tolerance. It appears, therefore, that the isoeffect curves for large and small volumes of brain (equations (1) and (2)) may slightly over-estimate the slope.

Figure 5 shows that for values of N between 10 and 31 the mean values for myelitis (2.5–35% incidence) and optic nerve and chiasm damage (>0 $<20\%$ incidence) are similar, and are situated midway between the two sets of empirically determined isoeffect curves for brain tolerance. Doses used for small volumes, therefore, may cause damage to spinal cord or visual pathways.

Figure 5 shows that the mean values for the series with lowest incidence of brain necrosis are higher than the corresponding values for myelitis and optic nerve and chiasm damage. However, the true incidence of brain necrosis in this series is unknown. As the values of "threshold" doses for brain necrosis are also higher (Table VI, see later discussion), it is probable that this complication is observed at slightly higher doses because it is a less sensitive end-point, rather than because of any fundamental difference in tissue response.

The very high doses in the hyperfractionation series (Table II) lie above the extrapolated values for empirically determined tolerance doses shown in Fig. 1, which as stated may have overestimated the slope slightly. As these high doses have not caused brain necrosis it is probable that "repopulation" has occurred between the widely spaced scedules, as has been described for radiation myelitis of the rat spinal cord (van der Kogel, 1977b; White and Hornsey, 1978).

The time–dose-fractionation equations derived from the data on five fractions per week available for whole and large volumes of brain combined (equation (3)), small volumes of brain (equation(4)), thoracic myelitis (equation (7)) and brain necrosis (equation (12)), all show a negligible exponent for T. The low dependence on T reflects the fixed relationship between N and T in the regimes examined, and also suggests that little recovery occurs during uninterrupted treatment regimes of five fractions per week.

The data on five fractions per week used to derive isoeffect curves for large and small volumes of brain (equations (1) and (2) and spinal cord (equation (7)) were examined in a relationship of *time* versus "dose" (in röntgens). The exponents for the power curves obtained were between 0.46 and 0.54. These are higher than the values of 0.22 used by Boden (1950) and 0.26 derived by Lindgren (1958) for brain tolerance and similar values quoted for spinal cord by Pallis *et al.* (1961), Maier *et al.* (1969), Vaeth (1965), Jellinger and Sturm (1971) and Palmer (1972).

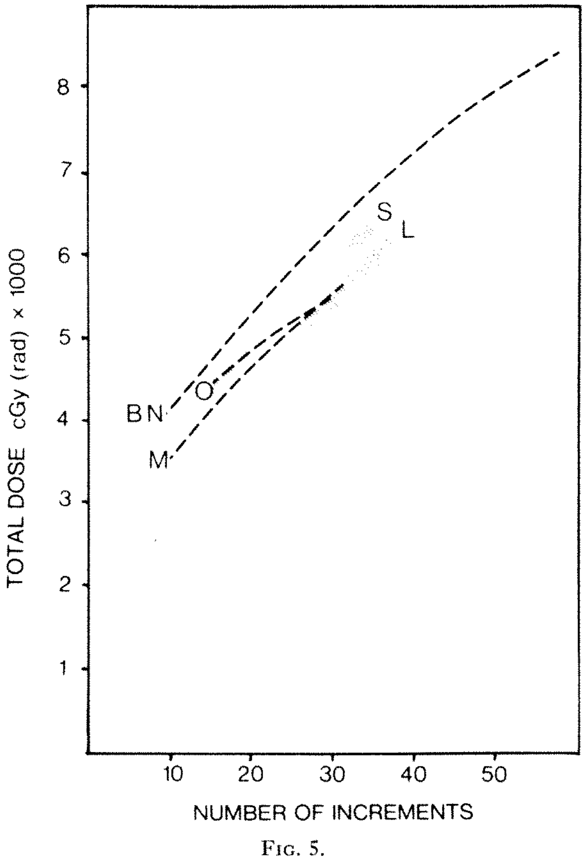


FIG. 5.

Isoeffect curves for mature human brain. 95% confidence limits of whole brain and large volumes of brain combined (L), and small volumes of brain (S), compared with mean tendencies of lowest (2.5–25%) incidence series of myelitis (M), optic nerve and chiasm damage $>0\%$ $<20\%$ (0), and brain necrosis with ED values <1541 ret (BN).

TABLE VI

TOLERANCE OF MATURE HUMAN BRAIN TO PHOTON IRRADIATION

Number of increments (N)	Empirically determined brain tolerance dose per increment (TD/N cGy (rad))		"Threshold" of tolerance, dose per increment (TD/N cGy (rad))		
	Large volume	Small volume	Thoracic myelitis	Optic nerve and chiasm damage	Brain necrosis
2	—	—	867	—	—
3	—	—	682	—	—
4	—	—	575	—	—
5	—	—	503	—	—
6	—	—	452	—	—
7	—	—	412	—	—
8	336	—	381	—	—
9	319	—	355	—	—
10	304	—	333	—	341
15	253	293	262	—	282
16	245	283	252	252	—
20	222	250	221	221	246
25	201	222	194	194	219
28	191	209	181	181	—
30	184	201	173	—	198
35	172	185	159	—	181
37	—	—	153	—	—
40	—	—	—	—	166

Intermediate values may be derived from equations (1), (2), (6) and Fig. 4.

Boden's isoeffect curve was derived by the inappropriate application of Strandqvist's (1944) curve derived from skin data. As the exponent for T is low (equations (3), (4), (7) and (12)), the dose per fraction becomes paramount, so that presenting data using overall time versus total dose as these authors have done, does not necessarily allow for differences in, or uncertainties of, dose per fraction, as with Palmer's (1972) and Jellinger and Sturm's (1971) series. Variation in overall treatment time, by departures from daily fractions or by use of split-course data (Lindgren, 1958; Maier *et al.*, 1969), have resulted in flatter isoeffect curves than occur when regular data on five fractions per week alone are used. The use of these inappropriately derived time–dose isoeffect curves has lead to persistant uncertainties regarding tolerance of brain and spinal cord.

The application of the Ellis equation derived from connective-tissue responses is inappropriate for central nervous tissue and may lead to substantial overdose. For example, a total dose of 5000 cGy (rad) given in 25 increments of 200 cGy (rad) at five fractions per week (1562 ret) lies within the empirically determined safe dose for large volumes of brain. The equivalent dose per fraction determined by the Ellis equation for 15 increments at five fractions per week is 277 cGy (rad). This is at the "threshold" of brain necrosis. The equivalent dose per fraction, determined for 15 fractions delivered in 25 days, is 295 cGy (rad). This exceeds the "threshold" for brain tolerance (Table VI).

In Table VI are examples of estimated mean values for brain tolerance derived from equations (1) and (2). This emphasizes the dependence of the tolerance of central nervous system tissue on dose per fraction. The dependence on dose per fraction for connective tissue is less, due to the lower exponent for N in the Ellis equation.

Examples of the best estimates of "thresholds" of tolerance for thoracic cord, and optic nerve and chiasm damage shown in Table VI are derived from equation (6). It is difficult to be certain of the dependency of dose on length of cord, but the data available are listed in Table III. Brain necrosis "thresholds" are derived from the lower 95% prediction limits of equation (10).

From the data available, there is considerable uncertainty regarding tolerance of central nervous system tissue when small numbers of fractions are used. The best guide available is the thoracic myelitis data. More information in this clinically useful range is particularly desirable, as is more information in the hyperfractionation region. In order to explore these deficiencies, animal experiments will be necessary. However, a plea is made for adequate documentation of treatment details when human data are reported.

ACKNOWLEDGMENTS

We wish to thank the following for assistance in the preparation of this paper: Drs. R. Kaye Scott, P. L. T. Ilbery, Mr. J. Drummond and Mrs. M. Blackwood; also the Anti Cancer Council of Victoria and the many radiotherapists visited at the centres listed in the appendix.

APPENDIX

Centres visited

Christie Hospital and Holt Radium Institute, Manchester; Glasgow Institute of Radiotherapeutics; Joint Centre for Radiation Therapy, Boston; McGill University, Montreal; M. D. Anderson Hospital and Tumor Institute, Houston; National Cancer Institute, Baltimore; Radiumhemmet, Karolinska Sjukhus, Stockholm; St. Luke's Hospital, Guildford; St. Bartholomew's Hospital, London; School of Medicine, University of California, San Francisco; The Royal Marsden Hospital, Surrey.

REFERENCES

Almquist, S., Dahlgren, S., Notter, G. and Sunbom, L., 1964. Brain necrosis after irradiation of the hypothalamus in Cushing's disease. *Acta Radiologica (Therapy)*, *2*, 179–188.

Aristizabal, S. and Caldwell, W. L., 1976. The relationship of time–dose factors to complications in the treatment of pituitary tumors by irradiation. *International Journal of Radiation Oncology Biology Physics*, *1*, 24–28.

Arnold, A., Bailey, P. and Harvey, R. A., 1954. Intolerance of the primate brainstem and hypothalamus to conventional and high energy radiations. *Neurology*, *4*, 575–585.

Atkins, H. L. and Tretter, P., 1966. Time–dose considerations in radiation myelopathy. *Acta Radiologica (Ther. Phys. Biol.)*, *5*, 79–94.

Boden, G., 1950. Radiation myelitis of the brainstem. *Journal of the Faculty of Radiologists*, *2*, 79–94.

Bouchard, J., 1966. In *Radiation Therapy of Tumors and Diseases of the Nervous System* (Lea & Febiger, Philadelphia).

Brenk, H. A. S. van den, Richter, W. and Hurley, R. H., 1968. Radiosensitivity of the human oxygenated cervical spinal cord based on analysis of 357 cases receiving 4 MeV Xrays in hyperbaric oxygen. *British Journal of Radiology*, *41*, 205–214.

Buys, N. S. and Kerns, T. C., 1957. Irradiation damage to the chiasm. *American Journal of Ophthalmology*, *44*, 483–486.

Coy, P., Baker, S. and Dolman, C. L., 1969. Progressive myelopathy due to radiation. *Canadian Medical Association Journal*, *100*, 1129–1133.

Crompton, M. R. and Layton, D. D., 1961. Delayed radionecrosis of the brain following therapeutic X-radiation of the pituitary. *Brain*, *84*, 85–101.

Dugger, G. S., Stratford, J. G. and Bouchard, J., 1954. Necrosis of the brain following roentgen irradiation. *American Journal of Roentgenology Radium Therapy and Nuclear Medicine*, *72*, 953–959.

Ellis, F., 1949. Radiotherapy in the treatment of pituitary basophilism and eosinophilism. *Proceedings of the Royal Society of Medicine*, *42*, 853–860.

1969. Dose, time and fractionation: a clinical hypothesis. *Clinical Radiology*, *20*, 1–7.

Field, S. B., Hornsey, S. and Kutsutani, Y., 1976. Effects of fractionated irradiation on mouse lung and a phenomenon of slow repair. *British Journal of Radiology*, *49*, 700–707.

Foltz, E. L., Holyoke, J. B. and Heyle, H. L., 1953. Brain necrosis following X-ray therapy. *Journal of Neurosurgery*, *10*, 423–429.

Forrest, A. P. M., Peebles-Brown, D. A., Morris, S. R. and Illingworth, C. F. W., 1956. Pituitary radon implant for advanced cancer. *Lancet*, *i*, 399–401.

Friedman, M. and Pearlman, A. W., 1955. Time–dose relationship in irradiation of recurrent cancer of the breast. *American Journal of Roentgenology Radium Therapy and Nuclear Medicine*, *73*, 986–998.

Ghatak, N. and White, B. E., 1969. Delayed radiation necrosis of the hypothalamus. *Archives of Neurology*, *21*, 425–430.

Harris, J. R. and Levine, M. B., 1976. Visual complications following irradiation for pituitary adenomas and craniopharyngiomas. *Radiology*, *120*, 167–171.

Hartog, M., Doyle, F., Fotherby, K., Fraser, R. and Joplin, G. F., 1965. Partial pituitary ablation with implants of gold-198 and yttrium-90 for Cushing's syndrome and associated adrenal hyperplasia. *British Medical Journal*, *ii*, 392–395.

Jellinger, K. and Sturm, K. W., 1971. Delayed radiation myelopathy in man. *Journal of the Neurological Sciences*, *14*, 389–408.

Jenkinson, E. L. and Oldberg, E., 1941. Results of conservative treatment in certain cerebral gliomas. *American Journal of Roentgenology and Radium Therapy*, *47*, 50–55.

Johns, H. E. and Cunningham, J. R., 1969. In *Physics of Radiology*, 3rd edit. (Charles C. Thomas, Springfield, Illinois), p. 458.

Kaplan, I. I., 1941. Irradiation of brain tumors at Bellevue Hospital 1924–1939. *Radiology*, *36*, 588–595.

Kaye Scott, R., 1978. Peter MacCallum Hospital, Melbourne. Personal communication.

Kjelberg, R. and Kliman, B., 1973. A system for therapy of pituitary tumors. In *Diagnosis and treatment of pituitary Tumors*. Ed. by P. O. Kohler and G. T. Ross (Excerpta Medica, Amsterdam), p. 234.

Kogel, A. J. van der, 1977a. Radiation tolerance of the spinal cord: time–dose relationships. *Radiology*, *122*, 505–509.

1977b. Radiation tolerance of the spinal cord: the dependence on fractionation and extended overall times. *IAEA Symposium on Radiobiological Research and Radiotherapy*, *1*, 85–90.

Kogel, A. J. van der and Barendsen, G. W., 1974. Late effects of spinal cord irradiation with 300 kV X rays and 15 MeV neutrons. *British Journal of Radiology*, *47*, 393–398.

Kogel, A. J. van der, Bekkum, D. W. and Barendsen, G. W., 1976. Tolerance of CNS to total body irradiation combined with chemotherapy applied for the treatment of leukaemia. *European Journal of Cancer*, *12*, 675–677.

Kramer, A., 1968. The hazards of therapeutic irradiation of the central nervous system. *Clinical Neurosurgery*, *15*, 301–318.

Kramer, S. and Lee, K. F., 1974. Complications of radiation therapy: the central nervous system. *Seminars in Roentgenology*, *9*, No. 1, 75–83.

Kramer, S., Southland, M. and Mansfield, C. M., 1968. Radiotherapy in the management of craniopharyngiomas. Further experiences and late results. *American Journal of Roentgenology Radium Therapy and Nuclear Medicine*, *103*, 44–52.

Lampert, P. W. and Davis, R. L., 1964. Delayed effects of radiation on the human central nervous system. *Neurology*, *14*, 912–917.

Lampert, P., Tom, M. I. and Rider, W. D., 1959. Disseminated demyelination of the brain following ^{60}Co gamma radiation. *Archives of Pathology*, *68*, 322–330.

Lindgren, M., 1958. On tolerance of brain tissue and sensitivity of brain tumors to irradiation. *Acta Radiologica, Supplement*, 170, pp.1–73.

Linfoot, J. A., Chong, C. Y., Garcia, J. F., Cleveland, A. S., Connell, G. M., Manougiam, E., Okerlund, M. D., Born, J. L., and Lawrence, J. H., 1971. Heavy particle therapy for acromegaly, Cushing's disease, Nelson's syndrome and non-functioning pituitary adenomas. *Progress in Atomic Medicine*, *3*, 219–237.

Locksmith, J. P. and Powers, W. E., 1968. Permanent radiation myelopathy. *American Journal of Roentgenology Radium Therapy and Nuclear Medicine*, *102*, 916–926.

Maier, J. G., Perry, R. H., Saylor, W. and Sulak, M. N., 1969. Radiation myelitis of the dorsolumbar spinal cord. *Radiology, 93*, 153–160.

Malamud, N., Boldrey, E. B., Welch, W. K. and Fadell, E. J., 1954. Necrosis of brain and spinal cord following X-ray therapy. *Journal of Neurosurgery, 11*, 353–362.

Marsa, G. W., Goffinet, D. R., Rubinstein, L. J. and Bagshaw, M. A., 1975. Megavoltage irradiation in the treatment of gliomas of the brain and spinal cord. *Cancer, 36*, 1681–1689.

Martins, A. N., Johnston, J. S., Henry, J. M., Stoffel, T. J. and Di Chiri, G., 1977. Delayed radiation necrosis of the brain. *Journal of Neurosurgery, 47*, 336–345.

Masuda, K., Reid, B. O. and Withers, H. R., 1977. Dose effect relationship for epilation and late effects on spinal cord in rats exposed to gamma rays. *Radiology, 122*, 239–242.

O'Connell, J. E. A. and Brunschwig, A., 1937. Observations on the roentgen treatment of intracranial gliomata with special reference to the effects of irradiation upon the surrounding brain. *Brain, 60*, 230–258.

Orth, D. N., 1973. In *Diagnosis and Treatment of Pituitary Tumors*. Ed. by P. O. Kohler and G. T. Ross (Excerpta Medica, Amsterdam), p. 269.

Pallis, C. A., Louis, S. and Morgan, R. L., 1961. Radiation myelopathy. *Brain, 84*, 460–479.

Palmer, J. J., 1972. Radiation myelopathy. *Brain, 95*, 109–122.

Paterson, R., 1960. The relative biological efficiencey of 20 MV and 4 MV radiations. *British Journal of Radiology, 33*, 271–286.

Peck, F. C. and McGovern, E. R., 1966. Radiation necrosis of the brain in acromegaly. *Journal of Neurosurgery, 25*, 536–542.

Pennybacker, J. and Russell, D., 1948. Necrosis of the brain due to radiation therapy. *Journal of Neurology, Neurosurgery and Psychiatry, 11*, 183–198.

Powell, M. J. D., 1965. A method for minimizing a sum of squares of non-linear functions without calculating derivatives. *Computer Journal, 5*, 303–308.

Reinhold, H. S., Kaalen, J. G. A. H. and Unger-Gils, K., 1976. Radiation myelopathy of the thoracic spinal cord. *International Journal of Radiation Oncology, Biology Physics, 1*, 651–657.

Rosengren, B., 1958. Two cases of atrophy of the optic nerve after previous roentgen treatment of the chiasmal region and the optic nerves. *Acta Opthalmalogica, 36*, 874–877.

Ross, H. S., Rosenberg, B. S. and Friedman, A. H., 1973. Delayed radiation necrosis of the optic nerve. *American Journal of Ophthalmology, 76*, 683–686.

Salazar, O. M., Rubin, P., McDonald, J. V. and Feldstein, M. L., 1976. Patterns of failure in intracranial astrocytomas after irradiation: analysis of dose and field factors. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 126*, 279–292.

Schatz N., Lichtenstein, S. and Corbet, J., 1975. Delayed radiation necrosis of optic nerve and chiasm. In *Neuro-ophthamology*, Ed. by J. S. Glaser and J. Lawton-Smith (C. V. Mosby, Saint Louis), Vol. 8, p.131.

Scholz, W. E. and Hsu, Y. K., 1938. Late damage from roentgen irradiation of the human brain. *Archives of Neurology and Psychiatry* (Chicago), *40*, 928–936.

Schukovsky, L. J. and Fletcher, G. H., 1972. Retinal and optic nerve complications in a high dose irradiation technique of ethmoid sinus and nasal cavity. *Radiology*, 104, 629–634.

Smithers, D. W., Clarkson, J. R. and Strong, J. A., 1943. The roentgen treatment of cancer of the oesophagus. *American Journal of Roentgenology and Radium Therapy, 49*, 606–634.

Spillane, J. C., 1951. Nervous and mental disorders in Cushing's syndrome. *Brain, 74*, 72–94.

Strandqvist, M., 1944. Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionieren. *Acta Radiologica, Supplement 5*, 1-300.

Todd, I. D. H., 1965. Choice of volume in the X-ray treatment of supratentorial gliomas. *British Journal of Radiology, 36*, 645–649.

Urdaneta, N., Chessin, H. and Fischer, J. J., 1976. Pituitary adenomas and craniopharyngiomas: analysis of 99 cases treated with radiation therapy. *International Journal of Radiation Oncology Biology Physics, 1*, 895–902.

Vaeth, J., 1965. Radiation-induced myelitis. In *Progress in Radiation Therapy*, Vol. 3, Ed. by F. Buschke (Grune & Stratton, New York), pp. 16-25.

Wachowski, T. J. and Chenault, H., 1945. Degenerative effects of large doses of roentgen rays on the human brain. *Radiology, 45*, 227–246.

Wara, W. M., Phillips, T. L., Sheline, G. E. and Schwade, J. G., 1975. Radiation tolerance of the spinal cord. *Cancer, 35*, 1558–1562.

White, A. and Hornsey, S., 1978. Radiation damage to the rat spinal cord: the effect of single and fractionated doses of X rays. *British Journal of Radiology, 51*, 515–523.

Book review

Management of Persons Accidentally Contaminated with Radionuclides. Recommendations of the National Council on Radiation Protection and Measurements (NCRP Report No. 65), pp. vi+205, 1980 (National Council on Radiation Protection and Measurements, Washington DC), $8.00.
ISBN 0-913392-49-9

This report is one of a series published by NCRP in which an authoritative American view is given on various matters connected with radiological protection. It has been written primarily to help physicians with responsibilities for the management of patients contaminated by radionuclides. The NCRP emphasise that the report is intended only as an aid or guide for dealing with accident cases in their initial stages and it is not therefore concerned with the purely clinical consequences of any such accidents.

The text is comprehensive, clearly written and supported by an extensive bibliography of over 400 references. A good account is given of the initial management of contaminated patients and the diagnostic techniques necessary to measure the extent of their contamination, while a most useful chapter of 37 pages reviews world experience of 18 of the most important radionuclides.

There is a valuable summary of practical measures in the chapter entitled "Quick reference information". In this, checklists are set out for on-site emergency procedures, history taking, decontamination measures and immediate therapy.

Accidents involving patients with substantial contamination by radionuclides are fortunately rare; perhaps because of this, textbooks on therapeutic medicine do not contain the information presented in this book. The NCRP has therefore done a most useful job and this report, together with ICRP Publication 28 which deals with the management of external exposure, should be on the bookshelf of every physician who may have to deal with patients who may have been exposed in this way.

S. Rae.

1981, *British Journal of Radiology*, *54*, 799–804

Repair during fractionated irradiation of the mouse bladder

By F. A. Stewart, BSc., Ph.D., V. S. Randhawa, B.Sc., B. D. Michael, B.Sc., Ph.D. and
J. Denekamp, B.Sc., Ph.D., D.Sc.

Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

(*Received February 1981*)

ABSTRACT

The capacity for repair of sublethal damage during fractionated irradiation of the mouse bladder has been measured. Graded doses of electrons were given as 1, 2 or 5 equal daily fractions.

Two functional end points were used to assess bladder damage: *a*) increased urination frequency and *b*) decreased bladder capacity. Repair of sublethal injury within 24 hours was found to be similar using both assays for bladder damage and was greater than the repair observed in mouse skin for a given dose per fraction.

The possibility of a slower repair process occurring in bladder was investigated by giving two fractions in increasing overall times (from 24 hours to one month). No increased repair was observed with the longer time intervals; hence there was no evidence for slow repair in the bladder.

The extent to which normal tissues are damaged during radiation treatment is of obvious clinical importance and in practice limits the total dose that can be delivered. Experiments on normal tissues have used animal lethality to measure radiation-induced failure of organ function (Hornsey and Vatistas, 1963; Phillips and Margolis, 1972) or clonal methods for assaying stem-cell survival (Till and McCulloch, 1961; Withers, 1967; Withers and Elkind, 1970). There are now also several non-destructive, functional assay systems available for normal tissues in rodents (Fowler *et al.*, 1965; Vatistas and Hornsey, 1966; Van der Kogel and Barendsen, 1974; Chauser *et al.*, 1976; Travis *et al.*, 1979) including our urination frequency assay for radiation damage in the mouse bladder (Stewart *et al.*, 1978). Since these assays are non-destructive they allow sequential testing of the same animals so that the time course for development of the reaction can be examined.

It is particularly important to measure the extent of injury to normal tissues after fractionated radiation treatments since the success of clinical radiotherapy regimes depends upon the ability of normal tissues to repair sublethal damage, and in some cases to replace depleted cells, during the course of treatment. Repair of sublethal radiation damage can be measured experimentally by comparing the doses required in single or fractionated treatments to produce equivalent levels of tissue damage. The present study was undertaken to measure repair of sublethal damage in mouse bladder using urination frequency and reduced bladder capacity (at sacrifice of the mice) as functional assays for radiation injury. This repair of sublethal injury, measured from dose-response curves, has been compared with the repair capacities reported for other normal tissues.

In addition to the "Elkind" type repair of sublethal injury, which is completed within 24 h, a slower repair process has been reported in some slowly dividing normal tissues such as lung and capillary endothelium (Field *et al.*, 1976; Reinhold and Buisman, 1975; Van den Brenk *et al.*, 1974). To investigate whether slow repair also occurs in the bladder, two equal doses of radiation were given with time intervals ranging from one day to one month and the repair increment for longer intervals was compared with that measured in 24 h.

MATERIALS AND METHODS

Bladders of female CBA mice, aged 8 weeks at the start of experimentation, were locally irradiated with electrons. Electrons were delivered, from a linear accelerator of 1.8 MeV nominal energy, at 75 pulses per second and approximately 25 mGy per pulse, i.e. an average dose rate of 112.5 Gy/min. The irradiation field size was 20 × 12 mm and doses quoted in this paper refer to the peak dose at 2–4 mm depth (the position of the bladder in female mice of this age). Groups of animals (6–10 per dose) were irradiated under sodium pentobarbitone anaesthesia (60 mg/kg), with a minimum of three radiation dose groups for each fractionation schedule; two and five fractions were given as equal daily doses. Full details of the irradiation set-up, procedures and dosimetry have been described elsewhere (Stewart *et al.*, 1978).

After treatment the mice were kept without testing for 6 months and then tested at approximately monthly intervals for urination frequency.

Urination frequency assay

Frequency measurements were made over a 24 hour period by housing mice in cages with a wire bar floor. Urine dropped through the bars onto absorbent paper which was drawn beneath the cages at a speed of 15 cm/h (Stewart *et al.*, 1978). At the end of a 24 hour test period the absorbent paper was removed and the number of urinations per mouse was scored. A 24-hour test period was chosen because of diurnal fluctuations in urination frequency, the results being averaged over the 24 hour period. In order to visualize urine spots more clearly the sheets were initially sprayed with a 0.5% solution of 4-di-methylaminobenzaldehyde in 1% HCl/ethanol to stain the urine bright yellow. However, it was subsequently found that ultraviolet light caused the urine to fluoresce and this proved to be an easier method of visualizing urine spots.

Urination frequency was measured at approximately monthly intervals from 6 to 15 months after treatment; previous experiments had demonstrated that there was no increase in frequency before six months (Stewart *et al.*, 1978). At 15 months individual urine volumes (excreted in 24 h) were calculated from the total area of urine on the absorbent sheets. Urine volumes were estimated using a calibration curve constructed for spots caused by dropping known volumes of urine (from the same strain and sex of mouse) onto the absorbent sheets.

Capacity technique

Fifteen months after irradiation the mice were sacrificed and the bladder volume was measured by inflating under modest pressure. Bladders of freshly killed mice were exposed, but left *in situ*, and a 25 gauge needle was inserted directly into the urethra which was then ligated. The needle was connected to a mercury manometer and increasing pressure (5 to 35 mm Hg) was applied. During inflation, bladders were kept moist with isotonic saline and the size was measured, in three dimensions at each pressure, using specially made calipers with fine stainless steel blades. From these measurements the bladder volume could be calculated as a function of increasing applied pressure.

Results

Urination frequency

Unirradiated control animals in this experiment had a very constant urination frequency (0.3 ± 0.1 urinations per mouse per hour) over the test period of 6 to 15 months. There was no increase in frequency in any of the irradiated animals at six or seven months after irradiation. Over the period eight to ten months, slight increases in urination frequency developed in some of the single-dose groups but a consistent dose-response effect was not observed until 12 months after irradiation. This is somewhat later than in previous experiments, in which a dose-related radiation response developed by nine months (Stewart *et al.*, 1978). There was more scatter than usual on the single-dose data in this experiment when tested at 15 months, which makes an accurate comparison with the two and five fraction dose response curves difficult. However, it was not possible to assess repair capacities at earlier times (when there was less scatter on the single dose curve) since urination frequency after two and five fractions was not maximal until 15 months. Figure 1 illustrates dose-response curves after one, two and five daily fractions. It is clear from the displacement of the fractionated curves that there was significant repair of sublethal injury in two and five fractions. For high-dose levels, repair increments of approximately 11 and 29 Gy respectively can be measured for two and five fractions.

A second series of experiments was performed to investigate the possibility of "slow repair" occurring in the bladder by varying the time interval between two equal fractions. Figure 2 illustrates values for single doses and 2F/24 h measured at 12 months after irradiation. The repair increment measured in this experiment is smaller (6–8 Gy) than the value obtained from the first experiment, perhaps as a consequence of the large scatter on the single-dose data illustrated in Fig. 1. Table I summarizes the repair increments with root mean square errors estimated from envelopes drawn around one SEM of each data point.

In Fig. 3 the curves for single doses and two fractions in 24 h are reproduced without data points. Urination frequency data for two fractions given in one, two or four weeks are indicated against these curves. These data fall close to the 2F/24 h line, suggesting that no additional repair occurred during the longer time intervals of one to four weeks.

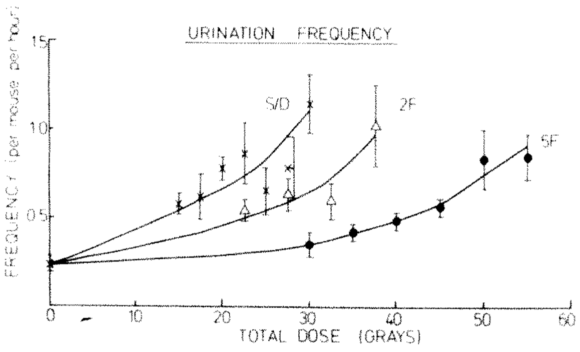


Fig. 1.

Urination frequency as a function of dose at 15 months after irradiation. Single doses X, 2 fractions △, and 5 fractions ●.

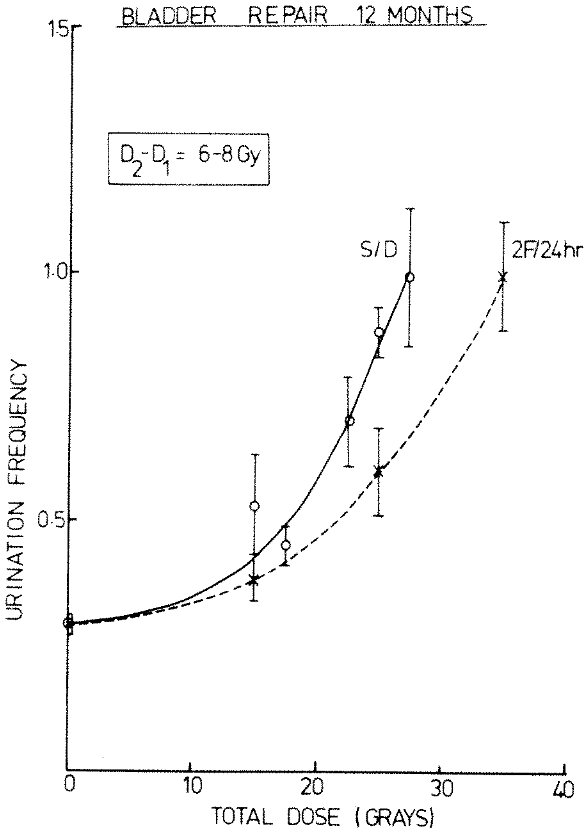


FIG. 2.

Each data point represents the mean value for a group of 6–10 mice ± 1SEM. Urination frequency data from experiment 2 at 12 months after irradiation for single doses (O) and 2F/24 hours (X). The ($D_2 - D_1$) value measured at frequency levels of 0.7–1.0 is shown on the graph.

TABLE I

REPAIR INCREMENTS FOR BLADDER

Treatment	D_N–D_1 (Gy) mean ± 1 SEM
2F/24h	
expt. 1 frequency	10 ± 2.3
expt. 1 capacity	7.6 ± 1.7
expt. 2 frequency	7 ± 0.6
expt. capacity	13 ± 1.5
5F/4d	
expt. 1 frequency	28 ± 6.5
expt. 1 capacity	24.5 ± 3.6

Repair measured from dose-response curves for urination frequency and for reduced bladder capacity at 15 mm Hg pressure. The values correspond to a threefold increase in frequency and a halving of the capacity. Root mean square errors have been obtained from envelopes drawn through the standard errors on all points contributing to each dose-response curve.

Bladder capacity

Figure 4 illustrates the extent to which bladder volume under increased pressure was reduced at 15 months after irradiation. The data demonstrate a progressive reduction in bladder volume, for a given pressure, with increasing radiation dose. Dose response curves were constructed from these data and the repair capacity was measured from a comparison of the single dose, two and five fraction experiments at 15 mm Hg applied pressure (Fig. 5).

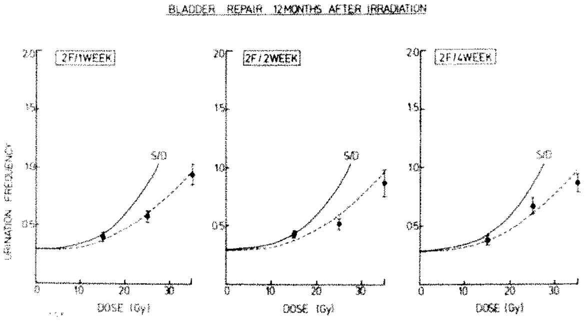


FIG. 3.

Urination frequency as a function of dose (12 months after irradiation). The solid and dashed lines represent the single dose and 2F/24 hour data from Fig. 2. Data points illustrate mean frequency values for 2F/1 week (left), 2F/2 weeks (centre) or 2F/4 weeks (right).

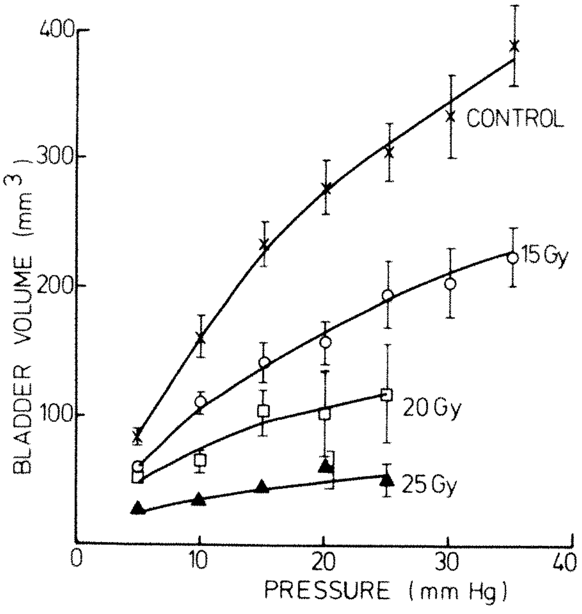


FIG. 4.

Bladder volume measured at increasing applied pressure. Data are shown for control animals (X) and a range of radiation doses at 15 months after treatment. Each point represents the mean volume of a group of mice ± 1SEM.

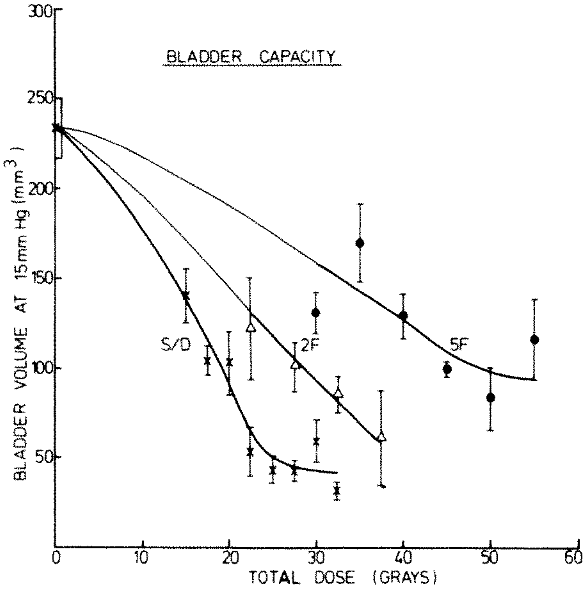


Fig. 5.

Dose response curves for bladder volume (at 15 mm Hg. applied pressure) after single doses (X), 2F (△) or 5F (●) treatments.

TABLE II

Dose (Gy)	Urine volume/24h (ml)
Control	1.42 ± .22
15	1.5 ± .15
17.5	1.4 ± .17
20	1.02 ± .24
25	0.54 ± .17
27.5	0.25 ± .05
30	0.56 ± .09
32.5	0.06 ± .02

Urine volumes for control and irradiated mice in a 24 hour period. Each value is the mean ± 1 SEM for a group of 6–10 animals. Volumes were estimated from the areas of urine per mouse on the absorbent frequency sheets. Urine output is significantly reduced after doses > 20 Gy.

This pressure was chosen because it caused a significant increase in bladder volume without bursting any of the fragile irradiated bladders. Repair increments measured from these curves are about 8 and 25 Gy for 2 and 5 fractions respectively. These values are in reasonably good agreement with the repair increments measured for the same mice by the urination frequency assay (Fig. 1 and Table I).

Discussion

Two separate assays (urination frequency and bladder volume) have been used to measure the extent of sublethal repair in the mouse bladder. The data confirm that dose-related increases in urination frequency are produced by electron irradiation of the bladder. At 12–15 months a moderately severe response (0.75 urinations per mouse per hour or 18 urinations in a 24 h period) resulted from a single dose of 23 Gy, 33 Gy in two fractions or 51 Gy in five fractions.

By 12 months after irradiation there is histological evidence of some fibrosis which could lead to decreased bladder capacity and increased frequency. We have also demonstrated that loss of epithelial cells coincides with the time of onset of increased urination frequency (Stewart *et al.*, 1980); at three months no increased urination frequency and little increased proliferative activity were observed in endothelium or epithelium. By 6–12 months marked increases in both proliferative activity and urination frequency were demonstrated. Proliferation rates remained high up to 19 months, which we interpreted as failure to replace the superficial epithelial cells, leaving deeper layers of tissue exposed and resulting in continued chemical irritation of unspecialized cells in contact with urine.

There is no evidence of a slow repair process occurring in the bladder, since repair between two fractions given in four weeks was no greater than repair in 24 h. This contrasts with data from some other slowly dividing normal tissues such as the lung and capillary endothelium (Field *et al.*, 1976; Reinhold and Buisman, 1975) where slow repair has been demonstrated. However, in the spinal cord (also a slow turnover tissue) no slow repair has been demonstrated; the sparing effect of extended fractionation was attributed entirely to repopulation (Van der Kogel, 1979).

Urination frequency has the advantage of being a non-destructive assay so that the same mice can be tested repeatedly over many months. However, the assay has the disadvantage that no account is taken of variations in urine volume which could occur if bladder irradiation influenced kidney function. The kidneys were not irradiated using the set-up described in this paper, but the ureters were included in the irradiation field which may have led to obstruction and back pressure to the kidneys, resulting in infection. We have observed a 10% incidence of hydro-nephrosis, with associated degeneration of kidney tissue at doses below 30 Gy and up to 60% after higher doses. It is clear from the measurements of urine volume in Table II that animals which had received radiation doses in excess of 20 Gy had significantly reduced urine outputs in a 24 hour period. Such variations in urine output will obviously influence the measured urination frequency;

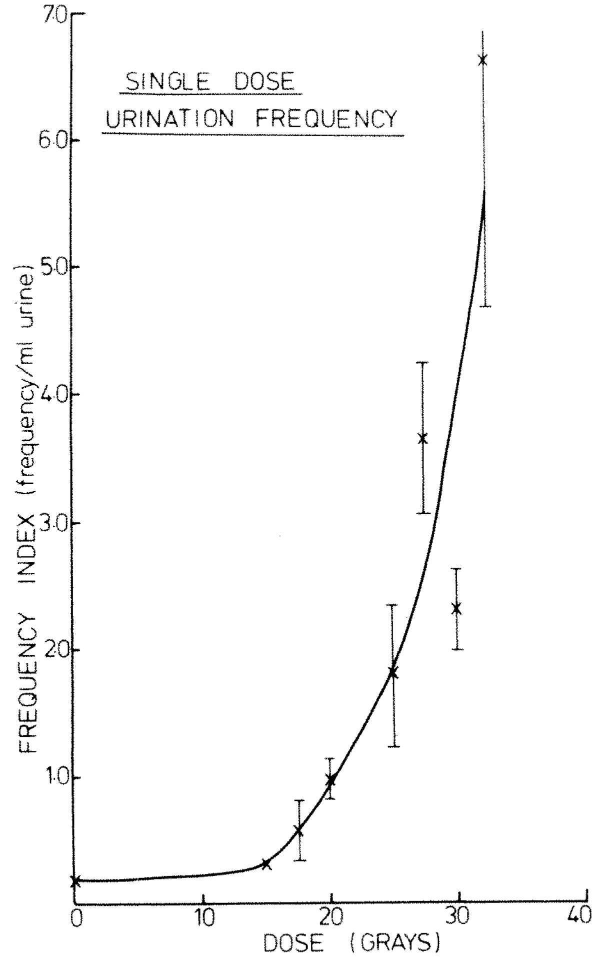


FIG. 6.

Frequency of urination corrected for the volume of urine excreted in 24 hours (frequency index) as a function of radiation dose. Each data point represents the mean frequency index for a group of 6–10 animals ± 1SEM. Frequency index values were derived from the urination frequency data illustrated in Fig. 1.

for mice producing very little urine, frequency may not be a good measure of radiation damage unless urine volume is taken into account. Single-dose data at 15 months after irradiation were therefore reanalysed as urination frequency/ml urine excreted (Fig. 6) which has the effect of considerably steepening the dose response curve, particularly at doses greater than 20 Gy. Unfortunately urine volumes were only analysed for the single-dose animals, so a similar retrospective correction of all of the data is not possible. In future experiments urine volumes will always be noted.

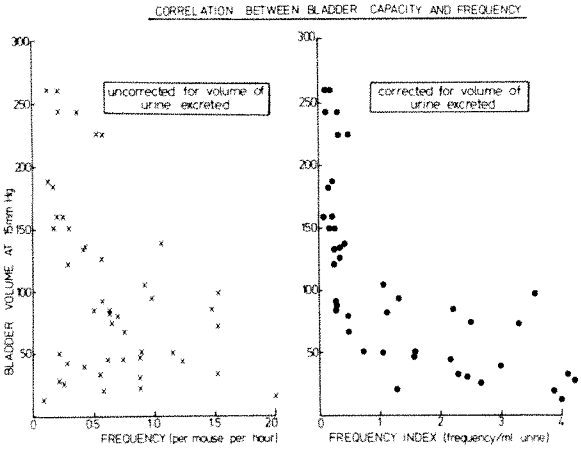


FIG. 7.

Bladder volume (at 15 mm/Hg) as a function of urination frequency (L) or frequency index (R). Only when the data are corrected for urine output (R) is there any correlation between bladder capacity and frequency.

In Fig. 7 the bladder volume at 15 mm Hg inflation pressure is plotted, for individual mice, as a function of urination frequency. When the number of urinations per mouse per hour (left hand panel) was used as the measure of frequency, there was no apparent correlation between volume and frequency. However, using frequency corrected for reduced urine output (right hand panel) there is some relationship between capacity and frequency; animals with a frequency index greater than 1.0 all had much less inflatable bladders with volumes less than 100 mm^3 at 15 mm Hg pressure.

Examination of dose-response curves (for urination frequency and reduced capacity) from single-dose and fractionated experiments allow us to estimate the extent of repair of sublethal radiation damage as a function of dose per fraction. In Fig. 8 the recovered dose per fraction interval $(D_N-D_1)/(N-1)$* has been plotted against the dose per fraction and compared with published values of recovered dose per fraction for mouse skin (Fowler *et al.*, 1972; Denekamp, 1973; Fowler *et al.*, 1974; Denekamp and Harris, 1975; Douglas and Fowler, 1976). All the dose values for bladder have been corrected by an RBE of 0.85 for electrons relative to 250 kV X rays (Lindop and Rotblat, 1961).

At low doses repair increments for bladder are only slightly higher than published values for skin but at higher doses three of the four sets of data indicate a much greater repair capacity in bladder than in skin. These estimated values for repair are also higher than published values for some other slowly dividing

---

*D_N = radiation dose in N fractions;
D_1 = dose in one fraction for equivalent tissue injury.

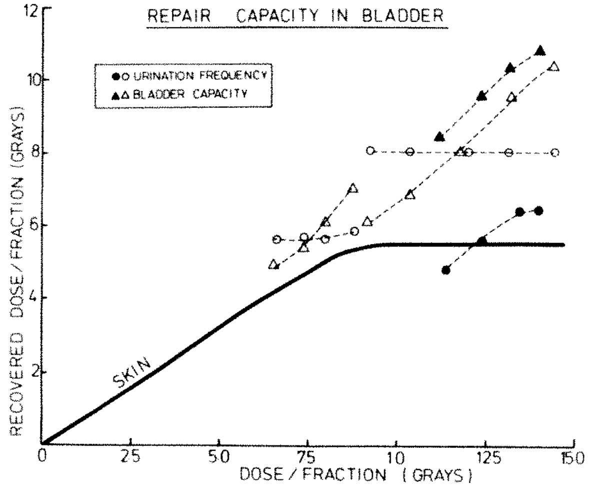


Fig. 8.

The dose increment needed to counteract repair between fractions $(D_N - D_1)/(N-1)$ as a function of the size of each radiation dose. The solid line represents published data for skin (see text). The data points and dashed lines illustrate repair for bladder measured from the urination-frequency dose-response curves (●, ○) illustrated in Fig. 1 and 2, or bladder-capacity (▲, △) illustrated in Fig. 5.

normal tissues. For doses per fraction of 7.5–10 Gy the recovered dose in bladder is 6–8 Gy per fraction compared with three and four Gy in lung and spinal cord respectively (Field *et al.*, 1976; Van der Kogel and Barendsen, 1974) and 5–6 Gy in mouse skin (Fig. 8).

Data presented in this paper demonstrate a lack of slow repair in the bladder. Repair of sublethal radiation injury (complete within 24 h) was however extensive. This would imply that, for the bladder, the number of fractions is much more important than overall time in determining tolerance dose to fractionated irradiation.

Acknowledgments

We would like to thank Prof. J. F. Fowler for many helpful discussions and criticism of this manuscript, Mr. P. Russell and his staff for care of the animals and the Cancer Research Campaign for financial support of this project.

REFERENCES

Chauser, B. H., Hudson, F. R. and Law, M. P., 1976. Renal function in the rat following irradiation. *Radiation Research, 67*, 86–97.

Denekamp, J., 1973. Changes in the rate of repopulation during multifraction irradiation of mouse skin. *British Journal of Radiology, 46*, 381–387.

Denekamp, J. and Harris, S. R., 1975. The response of mouse skin to multiple small doses of radiation. In *Proceedings of the 6th L. H. Gray Conference*, ed. T. Alper (Wiley, London), pp. 342–350.

Douglas, B. G. and Fowler, J. F., 1976. The effect of multiple small doses of X-rays on skin reactions in the mouse and a basic interpretation. *Radiation Research, 66*, 401–426.

Field, S. B., Hornsey, S. and Kutsutani, Y., 1976. Effects of fractionated irradiation on mouse lung and a phenomenon of slow repair. *British Journal of Radiology, 49*, 700–707.

Fowler, J. F., Denekamp, J., Delapeyre, C., Harris, S. R. and Sheldon, P. W., 1974. Skin reactions in mice after multifraction X-irradiation. *International Journal of Radiation Biology, 25*, 213–223.

Fowler, J. F., Denekamp, J., Page, A. L. and Begg, A. C., 1972. Fractionation with X-rays and neutrons in mice: Response of skin and C3H mammary tumours. *British Journal of Radiology, 45*, 237–249.

Fowler, J. F., Kragt, K., Ellis, R. E., Lindop, P. J. and Berry, R. J., 1965. The effect of divided doses of 15 MeV electrons on the skin response of mice. *International Journal of Radiation Biology, 9*, 241–252.

Hornsey, S. and Vatistas, S., 1963. Some characteristics of the survival curve of crypt cells of the small intestine of the mouse deduced after whole body X-irradiation. *British Journal of Radiology, 36*, 795–800.

Lindop, P. J. and Rotblat, J., 1961. Long term effects of a single whole body exposure of mice to ionizing radiations. I. Life-shortening. *Proceedings of the Royal Society of London, B, 154*, 332–368.

Phillips, T. L. and Margolis, L., 1972. Radiation pathology and the clinical response of lung and oesophagus. In *Frontiers of Radiation Therapy and Oncology*, Vol. 6, ed. J. M. Vaeth (Karger, Basel), pp. 254–273.

Reinhold, H. S. and Buisman, G. H., 1975. Repair of radiation damage to capillary endothelium. *British Journal of Radiology, 48*, 727–731.

Stewart, F. A., Denekamp, J. and Hirst, D. G., 1980. Proliferation kinetics of the mouse bladder after irradiation. *Cell and Tissue Kinetics, 13*, 75–89.

Stewart, F. A., Michael, B. D. and Denekamp, J., 1978. Late radiation damage in the mouse bladder as measured by increased urination frequency. *Radiation Research, 75*, 649–659.

Till, J. E. and McCulloch, E. A., 1961. A direct measurement of the radiation sensitivity of normal mouse bone marrow cells. *Radiation Research, 14*, 213–222.

Travis, E. L., Vojnovic, B., Davies, E. E. and Hirst, D. G., 1979. A plethysmographic method to test lung function in locally irradiated mice. *British Journal of Radiology, 52*, 67–74.

Van den Brenk, H. A. S., Sharpington, C., Orton, C. and Stone, M., 1974. Effects of X-irradiation on growth and function of the repair blastema (granulation tissue). II. Measurements of angio-genesis in the Selye pouch in the rat. *International Journal of Radiation Biology, 25*, 277–289.

Van der Kogel, A. J., 1979. Late effects of radiation on the spinal cord. Ph.D. thesis (TNO, Rijswijk).

Van der Kogel, A. J. and Barendsen, G. W., 1974. Late effects of spinal cord irradiation with 300 kV X-rays and 15 MeV neutrons. *British Journal of Radiology, 47*, 393–398.

Vatistas, S. and Hornsey, S., 1966. Radiation induced protein loss in the gastro-intestinal tract. *British Journal of Radiology, 39*, 547–550.

Withers, H. R., 1967. The dose-survival relationships for irradiation of epithelial cells of mouse skin. *British Journal of Radiology, 40*, 187–194.

Withers, H. R. and Elkind, M. M., 1970. Microcolony survival assay for cells of mouse intestinal mucosa exposed to radiation. *International Journal of Radiation Biology, 17*, 261–267.

1981, *British Journal of Radiology*, *54*, 805–807 SEPTEMBER 1981

Technical notes

A new technique for radiation shielding in superficial X-ray therapy

By B. Baily, M.Sc., *M. A. Coe, F.R.C.S. and T. M. Hearnden, M.Sc.

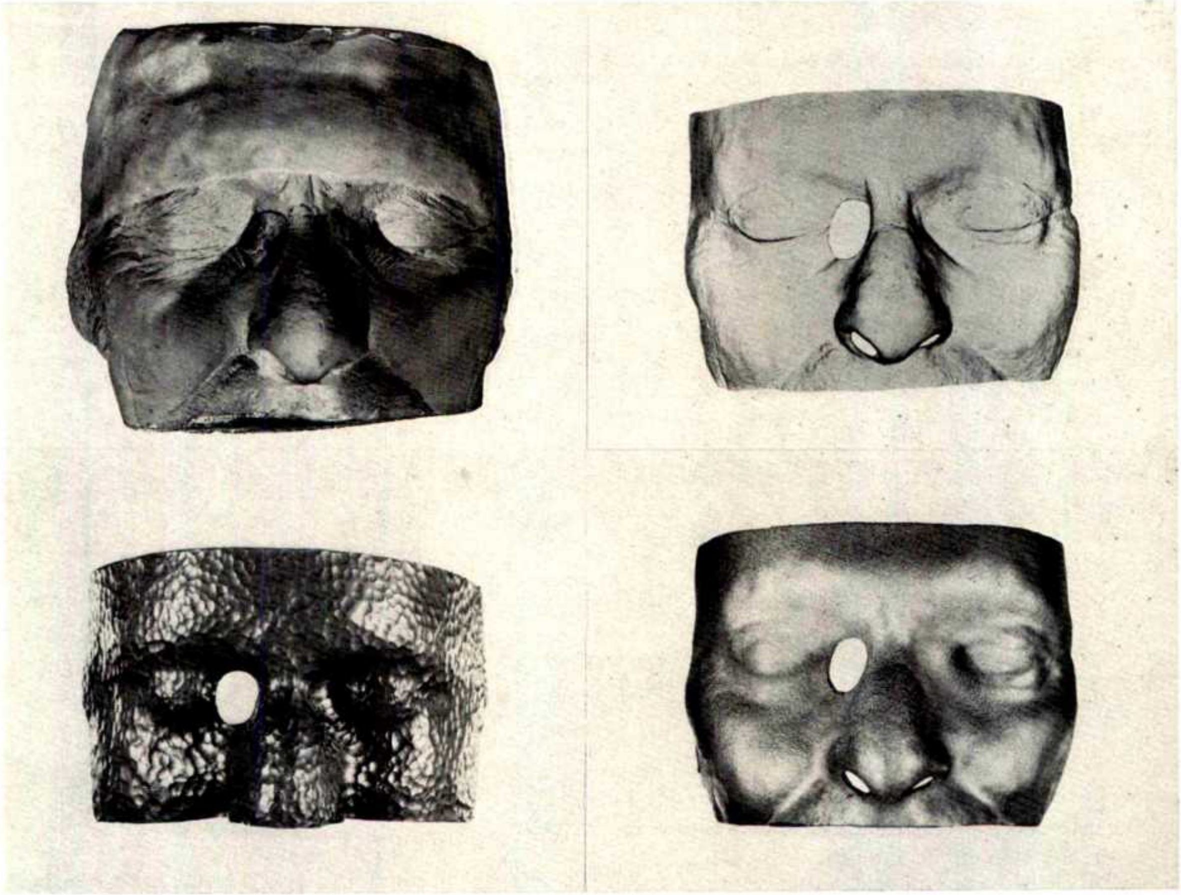
Physics and Radiotherapy Departments, Westminster Hospital, London S.W.1

(*Received April 1981*)

Lesions within the first few millimetres of the skin, such as basal-cell carcinoma, squamous-cell carcinoma and keloids, are commonly treated using X rays generated between 50 and 150 kV. The size and shape of such lesions are seldom identical with the applicators of the treatment unit and therefore it is necessary to shield uninvolved tissue.

When the area to be treated is reasonably flat the shielding can be readily cut from lead sheet backed with a thin layer of wax to absorb secondary electrons. However, if the body contour changes rapidly near the lesion, for example in some parts of the face, this method is not suitable.

In these circumstances the well-established method in use in many hospitals is to make a plaster-of-paris cast of the patient's face and beat a 1 or 2 mm thick lead sheet onto this cast until it fits (Fig. 1A). The area to be treated is cut out of the lead mask and the remainder coated in a suitable lacquer. Unfortunately, shaping lead in this way causes a



A FIG. 1. B

(A) Plaster of Paris cast (top). Lead mask (bottom). (B) "Darvic" shell (top). Alloy mask (bottom).

---

*Present address: Radiotherapy Department, St. Luke's Hospital, Guildford, Surrey.

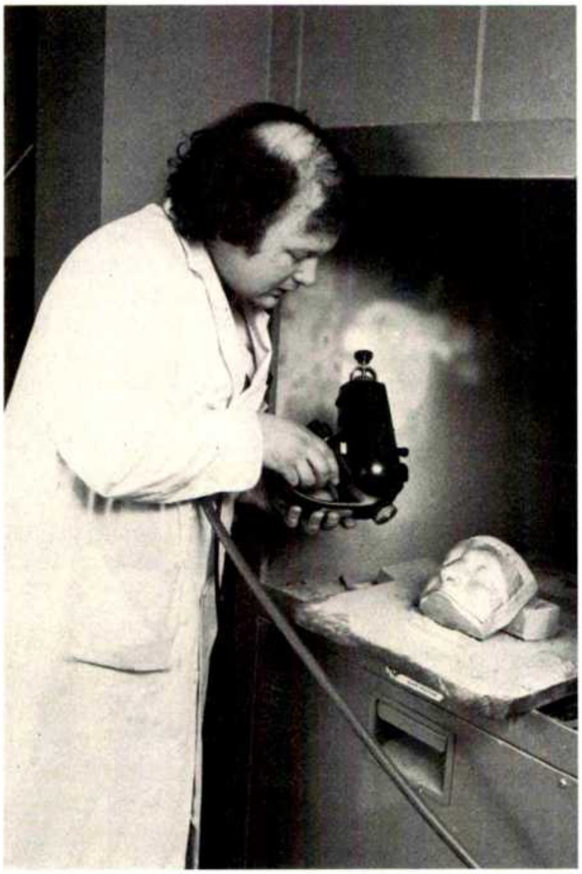


FIG. 2.
Spraying an alloy mask.

considerable reduction in thickness at points of sharp concave curvature, for example the inner canthus. This necessitates placing additional lead at such points. Furthermore, the whole process of shaping the lead face shield is very time-consuming, taking some 6–7 hours. To overcome these disadvantages a technique using low-melting-point alloys has been devised.

MATERIAL AND METHODS

Low-melting-point alloys are in widespread use as high-energy shielding blocks for mantle and other megavoltage treatments. MCP 70† is used extensively at Westminster Hospital for this purpose and similar alloys are used in an injection-moulding process which involves spraying molten alloy from a special heated compressed-air gun, shown in Fig. 2.

The same technique can be used to spray a plaster cast with molten alloy to make a mask. To provide absorption of secondary electrons, a 0.5 mm thick "Darvic"‡ shell (Fig. 1B) is first vacuum-formed on the cast. The alloy is then sprayed onto the shell which remains in position on the cast. A fine spray should be used to get a good impression and to produce a small grain structure as the alloy thickness is built up to between 2 and 3 mm. This results in a smooth homogenous mask (Fig. 1B). It is important to avoid a coarse, grainy structure as this can give rise to small perforations, particularly around areas of sharp convex curvature.

The final thickness depends on the X-ray energy, the need to ensure adequate coverage at points of sharp curvature, and the need to keep weight to a reasonable level. The practical minimum thickness required for adequate strength and coverage is about 2 mm. Extra thickness can be built up locally wherever necessary. The Darvic shell gives additional strength, allows the mask to be lifted without damage and provides a comfortable, hygienic surface for contact with the patient.

The area to be treated is then cut out of the alloy mask and Darvic shell. This is conveniently and accurately done by first placing the transparent shell only on the patient's face and drawing on it the outline of the area to be treated with a sharp wax pencil. The outline is easily transferred to the alloy mask. Figure 3 shows a mask in use.

RESULTS

A number of alloys of varying lead content and melting-point are available from Mining and Chemical Products. Those listed in Table I were tested in the form of flat sprayed sheets at 75, 150 and 250 kV. The transmission curves obtained, together with those measured for lead, were used to derive the tenth-value-layers and "MCP equivalents" given in Table I. Sample densities were found by weighing and displacement, both for the flat sheets and samples taken from actual masks. The spraying process produces no significant reduction in density compared with the cast alloy.

The effectiveness of the shielding was confirmed by irradiating several casts complete with MCP 70 masks and using LiF dosimeters ($3.2 \times 3.2 \times 0.9$ mm chips) to measure the transmitted dose at various points. Maximum transmission at 250 kV was found to be about 10% of the incident dose.

DISCUSSION

The technique of spraying masks for superficial X-ray therapy produces a perfectly fitting shield

---

†Mining and Chemical Products, 11 Margaret Street, Stone, Staffs. ST15 3EQ.

‡P.V.C. sheet; ICI Ltd.

TABLE I

PROPERTIES OF LOW-MELTING-POINT ALLOYS

Alloy	Composition	M.P. (°C)	Density† (gm/cm³)	Tenth-value-layer (mm)			"MCP equivalent"*		
				75kV	150kV	250kV	75kV	150kV	250kV
MCP 69	Bi/Pb/Sn/Cd	69	9.7	0.2	0.7	1.9	1.1	1.3	1.5
MCP 70	Bi/Pb/Sn/Cd	70	9.67	0.3	0.8	2.0	1.3	1.6	1.6
MCP 124	Bi/Pb	124	10.73	0.3	0.7	1.7	1.3	1.3	1.3
MCP 137	Bi/Sn	138	8.58	0.2	0.9	2.8	1.4	1.7	2.1
Lead	Pb	327	11.3	0.2	0.5	1.3	—	—	—

*The term "MCP equivalent" indicates the thickness of alloy (mm) equivalent to 1 mm lead.
†Manufacturer's values for cast alloy.
Note: The X-ray beams had the following characteristics:
75 kV, 20mA, 2 mm Al inherent filtration, 2.03 mm Al HVL.
150 kV 20 mA, 0.5 mm Cu added filtration, 0.76 mm Cu HVL.
250 kV, 15 mA, 0.4 mm Thoracus filter, 3.04 mm Cu HVL.

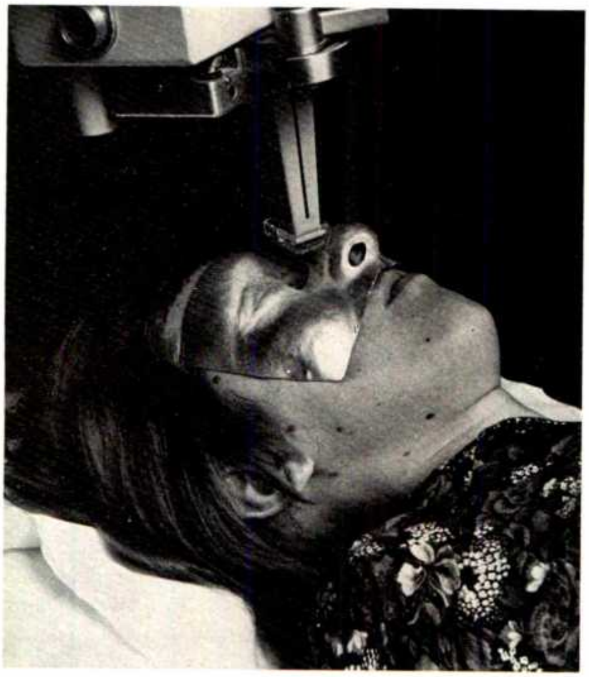


FIG. 3.
Example of an alloy mask in use.

(Fig. 3). This means that the exact area marked up for treatment is being treated every time. The method is effective and quick, taking about one hour. It is cheap in terms of materials, because the mask is recycled once treatment is finished, and particularly so if the alloy is already in use for megavoltage shielding.

It can be seen from Table I that the tin content of MCP 137 (K-edge=30 keV) has an effect at 75 kV but the two lead alloys, MCP 70 and MCP 124, are more effective over the whole energy range. MCP 124 affords slightly better shielding and more uniform properties. However, MCP 70 was chosen for spraying masks since it was already in use at Westminster Hospital for megavoltage shielding. The very recently introduced MCP 69 affords virtually identical shielding but is slightly cheaper and has superior properties for casting.

The spray gun and spraying booth, essential to protect the operator from dust and to reclaim waste, are expensive items but will perform other useful functions in a large workshop.

ACKNOWLEDGMENTS

We wish to thank Mr. John Rose, Senior Technician, for first suggesting the idea and for spraying the early prototypes. We are indebted to Mr. Malcolm Chapman, Mould Room Technician, for producing the many casts, shells and masks required. Mr. L. Morrison of Mining and Chemical Products gave invaluable advice and demonstrations on spraying technique and provided the flat sheets for testing.

1981, *British Journal of Radiology*, 54, 808-812

Technical notes

A transportable gamma camera service: initial technical results

By M. A. Smith, B.Sc., M.Sc., Ph.D., M. V. Merrick, M.A., B.M., F.R.C.R., V. F. Storjohann, D.C.R. and A. J. Wong, B.Sc.

Departments of Medical Physics and Medical Engineering and Medical Radioisotopes, Western General Hospital, Edinburgh

(Received December 1980 and in revised form April 1981)

The relatively high cost of nuclear-medicine equipment has produced a situation in which a service is provided centrally, patients being transferred from smaller or outlying hospitals. The disadvantages of inter-hospital transfer of the ill patient, the inability to perform investigations on those too ill to travel, and the man-hours involved escorting patients, prompted this study to assess both the technical feasibility and the possible clinical advantages of providing a transportable nuclear-medicine service. This paper is concerned solely with technical aspects of the project, concentrating on its initial design and the results obtained in the first six months.

At the planning stage in 1977 a choice had to be made between transporting a mobile gamma camera which could be off-loaded from a small van and driven into the hospital, or a static gamma camera permanently positioned in a large van, similar to the mass X-ray service or mobile whole-body counter (Boddy, 1967). The former approach was adopted for the following reasons: the quality of images from a mobile gamma camera was as good as that of images from a static camera, the transporting vehicle would be much cheaper, the driver would not require an HGV licence and finally the patients would not have to be brought outside the hospital.

EQUIPMENT

Mobile gamma camera

A camera with on-board processing was considered essential if an adequate service was to be provided. At the time only two were on the market in this country. The Elscint Dymax MB was chosen mainly because of its superior manoeuvrability, its larger field of view and its ease of operation.

The Dymax-MB has a 30 cm field of view camera mounted on a chassis with a modified Dycomette data processor using a Nova 3/4 minicomputer and was designed for use within a hospital. Many of the display features are "hard-wired" and the data and programmes are stored on floppy discs. The mobile camera is driven and steered by a fifth wheel centrally positioned at the rear. There are three forward speeds and three reverse (max. 4 m.p.h.). Safety cut-outs are operated by the front and rear bumpers and steering column. The latter also works on a "dead man's handle" principle. The total cost of the mobile gamma camera was £81 658.

To protect the NaI crystal against thermal shock, a removable insulating "cosy" was made from 1.2 cm thick high-density foam which completely surrounded the head. Two resistance thermometers were connected to a chart recorder which was attached to the mobile gamma camera and powered from its batteries. One measured the ambient temperature on the camera yoke and the other the temperature inside the "cosy" adjacent to the collimator. Thus the precautions taken against thermal shock to the crystal could be evaluated. A plastic cover was specially made to fit completely over the mobile camera to protect it from rain when out of doors. The only modification made to the mobile camera was the removal of 45 kg of lead from over the drive wheel. This did not impair the performance of the mobile, except when driving over very rough ground, and reduced the weight to approximately 1040 kg.

Transporting vehicle

A specially designed body was built on a 1750 kg (35 cwt) Bedford chassis fitted with unmodified heavy-duty suspension, this being the smallest that could carry the necessary weight. For loading and unloading two methods were considered; a hydraulic tail lift or a ramp and winch system. The former appeared the most desirable method for both speed and ease of operation but had to be rejected on grounds of cost. The mobile camera could only be supported by a conventional tail lift on a large van, or by a more expensive non-standard tail lift with hydraulic jacks on all four corners on a small van.

The ramp and winch system used to load and unload the mobile camera is shown in Figs. 1 and 2. When describing the system, "front" refers to the direction towards the driver's cab. The mobile camera had a transverse wheel base of 0.61 m and a ground clearance of 7.5 cm. It is initially driven on to a steel trolley with a transverse wheel base of 1.08 m, the rear wheels of which pivot vertically so that the rear edge can rest on the ground. Once on the trolley,

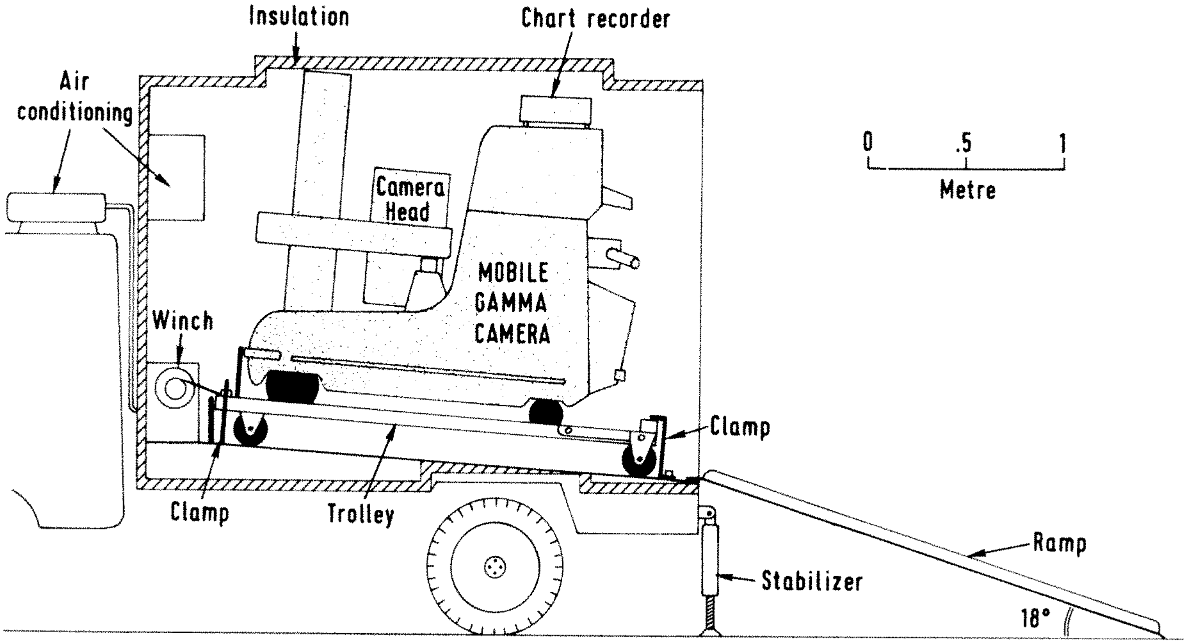


FIG. 1.
Diagram showing interior of the van with mobile camera loaded.

brackets are placed in the ends of the box section of the mobile camera's chassis, one in each corner, and bolted to the floor of the trolley. A hand operated hydraulic jack is then used to raise the rear of the trolley until it is horizontal, when steel pins are inserted to fix the rear wheels into position. An 8 mm diameter steel cable is attached from the winch to the front of the trolley.

A 12 V d.c. electric winch with 3600 kg (8000 lb) capacity is operated by a switch at the rear of the van. It is powered by the van's batteries, but the van's engine must be running during loading. The trolley is pulled up the ramps and into the van, the floor of which is slanted to reduce the angle between the floor and ramps at the rear of the van. This could not be achieved by increasing the length of the ramps because they have to fit inside the van to be transported. Once fully winched into the van the trolley is secured at the front on both sides and in the centre at the rear. The camera is thus transported securely bolted to the trolley which is in turn secured to the floor of the van.

During loading and unloading, stabilizers are attached to the rear of the van to give support just before the rear suspension is fully loaded. Like the ramps, these too are removed and stored inside the van. The time taken from the mobile camera being driven out of the hospital until the rear doors of the van are closed is about five minutes when two operators are present.

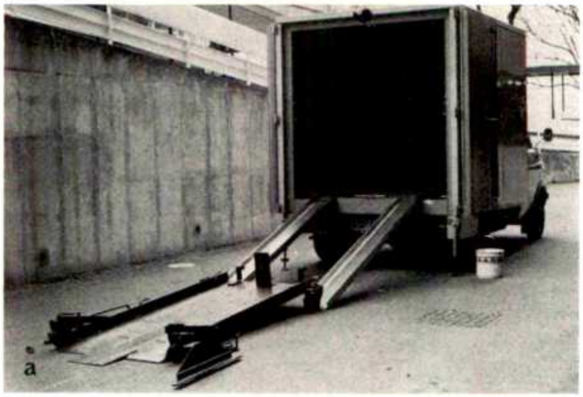
The van is fitted with an air-conditioner unit which operates via its engine, and 75 mm of polystyrene insulation fitted around the body. Such precautions were felt imperative to protect the crystal against the more inhospitable elements of a Scottish winter. As an added precaution against collision with other motor vehicles, the van was painted bright yellow. The total cost of the van plus all the modifications was £11 990.

TRANSPORTABLE MOBILE GAMMA CAMERA SERVICE

Organization

The mobile camera was delivered at the end of March 1979 but the van was not ready until January 1980. During this time, however, the two members of staff employed with the project, a superintendent radiographer and a medical physics technician grade III, became familiar with all aspects of the camera and processor whilst it was in use in the central department at the Western General Hospital. The service started in January 1980 with visits to five hospitals in the locality, each for one day per week (Fig. 3). A route was chosen to minimize the distance travelled by the camera which is left overnight in three of the hospitals, the van returning every day to the central hospital.

The radioisotopes for the patients who have been booked plus additional ^{99}Tc^{m}MAA are taken each day in the van to the hospital visited. The rooms in which the mobile is used in each of the five hospitals vary in size from 5 m^2 to 22.5 m^2. In the case of the smallest room, the camera head protrudes through the entrance and the patient is positioned outside the door. All studies, both static and dynamic, are recorded on floppy disc but are processed before leaving the hospital. The processed scans are returned to the central hospital at the end of the day and are reported by the nuclear-medicine consultant with reference to the original data on disc when necessary. All radioactive waste is also returned each day to the central hospital.



Initial experience

During the first six months of the service, from January to October, the mobile camera travelled over 3700 km (2300 miles) and was loaded or unloaded more than 210 times in all weather conditions.

The main concern was whether the NaI crystal could withstand the temperature gradients to which the mobile would be exposed. The camera was never taken out of a hospital without a collimator in position and the insulating cosy surrounding the head.

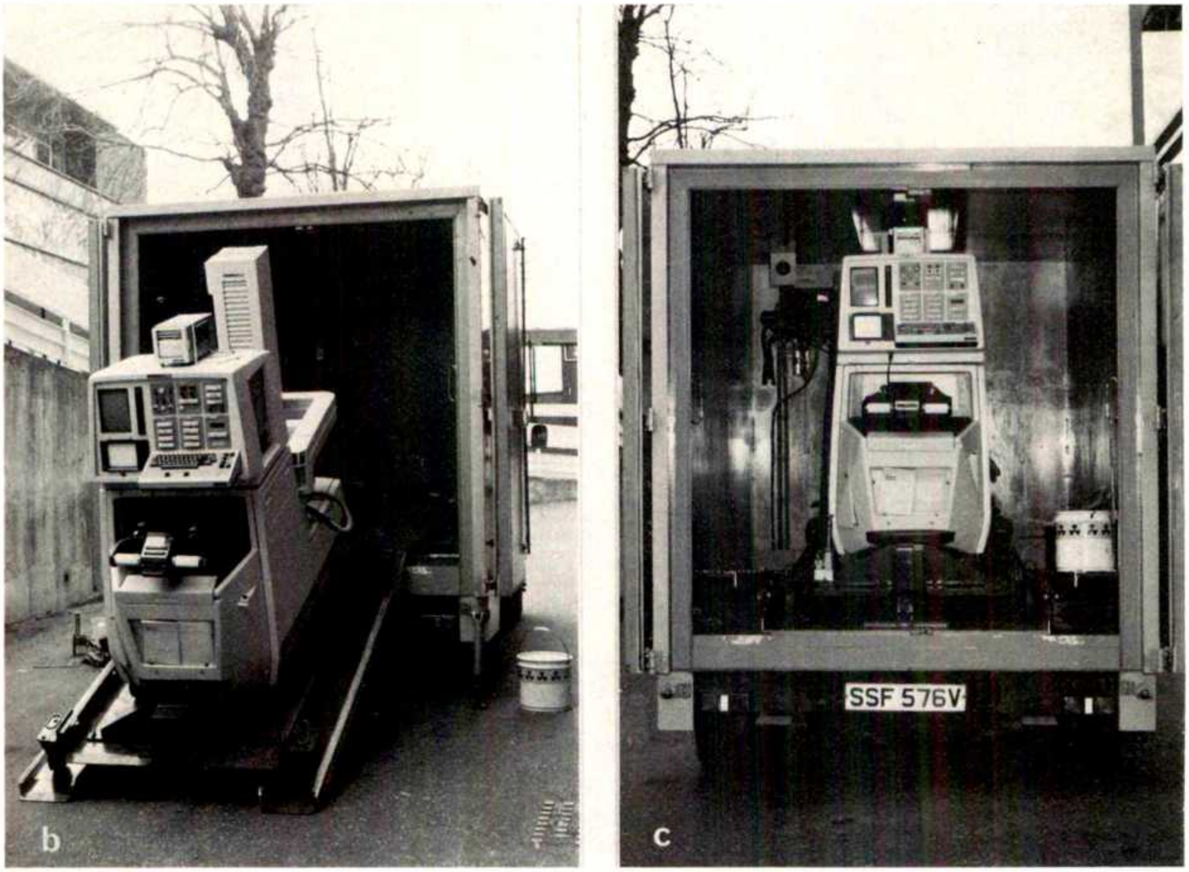


Fig. 2.

Three stages during the loading of the mobile camera.

(a) Rear of trolley rests on ground so that mobile camera can be driven on.

(b) Mobile camera on the trolley is winched into van.

(c) Trolley clamped in position, ramps, stabilizers and isotopes loaded either side.

The temperature was monitored as described previously during the critical period from mid-January to the beginning of April. The results are shown in Fig. 4. The average time for each journey was just over one hour and the temperature gradient inside the cosy never exceeded the manufacturer's maximum of 5°C/h. The average maximum temperature difference between the two thermometers on any one day was 9.4°C with a maximum of 16°C.

The integral uniformity was measured daily once the mobile camera was in the peripheral hospital (Fig. 5). A 3 cm square (10% field of view) was used so that comparisons could be made with the manufacturer's specifications. The average integral uniformity was ±7.79% with a standard deviation of 1.42. As can be seen, the uniformity remained reasonably constant and did not deteriorate. Qualitative assessment of the resolution using an Anger phantom and quantitative measurements of the sensitivity using a small circular phantom (HPA report, 1978) showed that neither characteristic changed significantly.

During the first six months the service had to be suspended for a variety of reasons. Six days were lost solely due to faults developing on the mobile camera and two days because the battery had not been charged overnight. The provision of a technician working with the mobile camera enabled many minor faults which developed whilst at a peripheral hospital to be repaired immediately. Only one day was lost because of bad weather. Modifications to the van caused the greatest interruption in the service. It was found that the loaded van exceeded its plated weight (3.56 tonnes) by about 100 kg and so had to be modified to bring the loaded weight down to 3.33 tonnes. Other days were lost due to improvements made to the mobile camera by Elscint and to staff holidays.

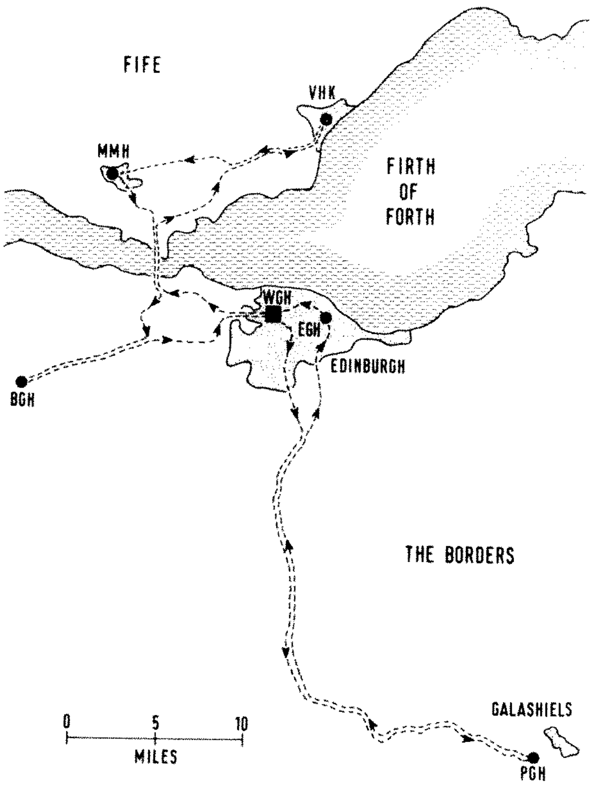


Fig. 3.

Route travelled by mobile camera. Monday morning from the Western General Hospital (WGH) to the Victoria Hospital, Kirkcaldy (VHK), then in the late afternoon to Milesmark Hospital (MMH) Dunfermline. Tuesday afternoon from MMH to Bangour General Hospital (BGH). Wednesday afternoon from BGH back to the WGH. Thursday morning from WGH to Peel General Hospital (PGH), Galashiels, then in the afternoon to the Eastern General Hospital (EGH). Friday afternoon back to the WGH.

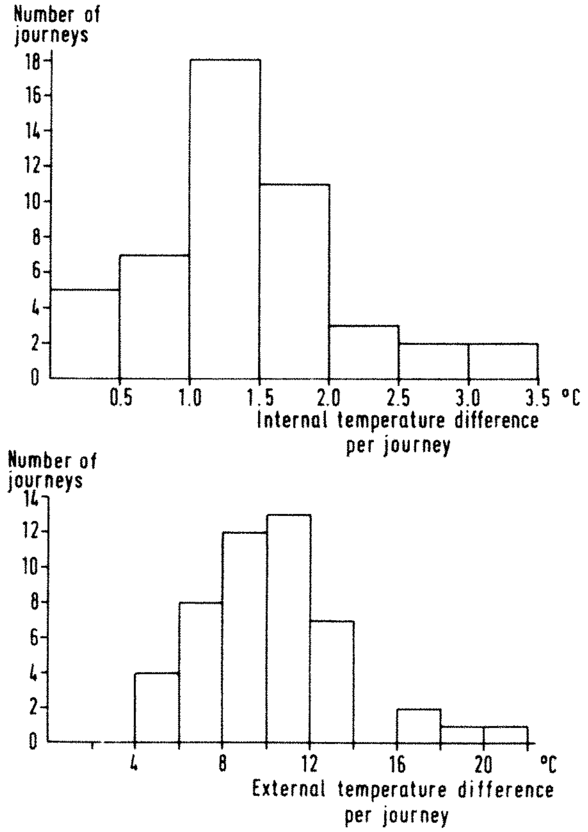


Fig. 4.

Histograms of temperature differences (max-min) adjacent to the collimator (internal) and on the camera yoke (external) during first three months of 1980. Data from approximately 77 hours of recording whilst the camera was in transit.

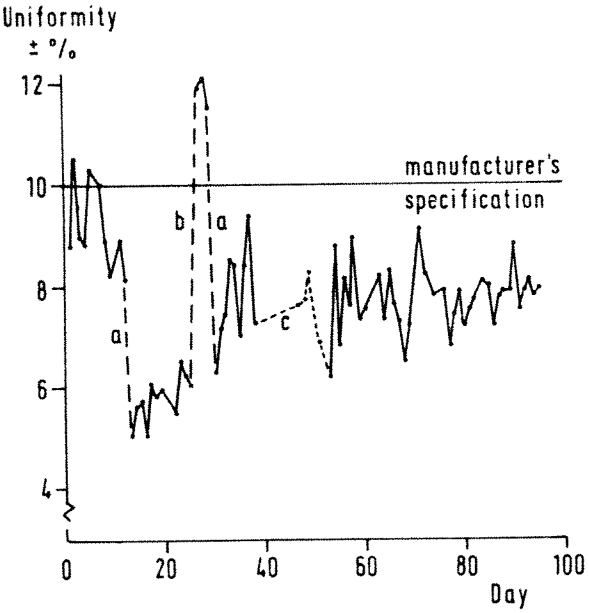


Fig. 5.

Variations in daily integral uniformity measurements. (a) Uniformity adjusted by technician. (b) Uniformity following a service visit. (c) Single operator only so daily measurements suspended.

The possibility of the service being provided by a single operator was investigated over a two week period. Although it is possible for a single person to load and unload the camera, it is heavy work and impractical in bad weather. The strain and responsibility of loading and unloading the mobile camera, driving the van plus performing the patient scans were found to be unacceptable for one person.

The revenue cost of the service for the first six months of this financial year was as follows: £6475 for staff salaries, running the van and incidentals, and £3450 for the camera maintenance contract

Conclusions

The initial results from this study demonstrate that a routine transportable gamma-camera service can be provided. The ability of a mobile camera to withstand both the mechanical and thermal shocks whilst travelling distances of up to 130km (80 miles) per day in most weather conditions has been shown. We disagree with some of the conclusions regarding the thermal protection of the camera contained in a previous study (Elliot *et al.*, 1979). The cost of insulating the head is minimal and should be borne; the desirability of air conditioning is partly dependent on the distances to be travelled. However it could prove a reasonable precaution even on short journeys in the event of a breakdown. Heating would be much cheaper, but we were unable to find any heating system with adequate safeguards against overheating.

The method of loading and transporting the mobile camera works successfully, but has two disadvantages. Firstly, to provide a service the allocation of a third member of staff is necessary to cover for holidays and illness. Secondly the van is a limited investment. Had more money been spent initially on a larger van with a tail lift, one person could easily have loaded and unloaded the camera eliminating the need for a third member of staff. If such a van were used, care should be taken to ensure that the loaded weight does not exceed that for which a HGV licence is required.

Acknowledgments

The authors would particularly like to thank: Mr. S. D. P. Black of the Scottish Motor Traction Co.; the radiologists concerned, namely: Dr. P. Aitken, Dr. I. Houston, Dr. S. McCall-Smith, Dr. D. Smith and Dr. K. Wood, and the Chief Administrative Medical Officers of the Borders, Fife and Lothian areas; Dr. J. D. Simpson, Principal Physicist; and the Scottish Home and Health Department for funding the project.

REFERENCES

Boddy, K., 1967. A high sensitivity shadow-shield whole body monitor with scanning-bed and tilting chair geometries, incorporated in a mobile laboratory. *British Journal of Radiology*, *40*, 631–637.

Elliot, A. T., Nottage, C. F., Newcombe, P. B. and Britton, K. E., 1979. The provision of a district nuclear medicine service. *British Journal of Radiology*, *52*, 419–420.

Hospital Physicists' Association, 1978. H.P.A. Topic Group Report 27: The theory, specification and testing of Anger type gamma cameras, (H.P.A., London).

1981, *British Journal of Radiology*, *54*, 813–815

Case reports

Retroperitoneal angiomatous lymphoid hamartoma demonstrated by ultrasound

By S. Hamilton, B.A., D.M.R.D., F.R.C.R. and D. McInerney, M.D., M.R.C.P., F.R.C.R.

Department of Radiology, Meath Hospital, Dublin 8

(Received November 1980 and in revised form January 1981)

Angiomatous lymphoid hamartomata are rare tumours occurring occasionally in the abdomen. Conventional radiological investigations are inconclusive and diagnosis has usually been made on examination of the excised specimen. The ultrasound appearances which have not been previously reported are described here.

CASE REPORT

A woman aged twentyfour had complained for two months of a swelling in the right side of her abdomen. This became tender during menstruation. She was otherwise asymptomatic.

A large, smooth, firm, mobile mass was palpated in the right flank. Routine pathological tests of blood and urine were normal. At urography, obstruction of the upper third of the right ureter by a large soft tissue mass in the right flank was shown (Fig. 1).

Barium studies showed a normal small bowel and upward and lateral displacement of the right side of the colon by an extrinsic mass (Fig. 2). Selective superior mesenteric angiography showed displacement of adjacent normal vessels and that the mass was virtually avascular with only a few small vessels supplying it (Fig. 3). Ultrasound was performed with a commercially available grey-scale B-mode scanner using 2 mHz and 4 mHz focussed transducers. This showed a well-defined mass, 17 cm in maximum diameter, lying antero-inferior to the right kidney and adjacent to the inferior surface of the liver. The mass was chiefly echogenic but contained round anechoic areas with distal echo enhancement consistent with cysts (Figs. 4 and 5). A gall-bladder calculus was present. No other abnormality was shown on scanning.

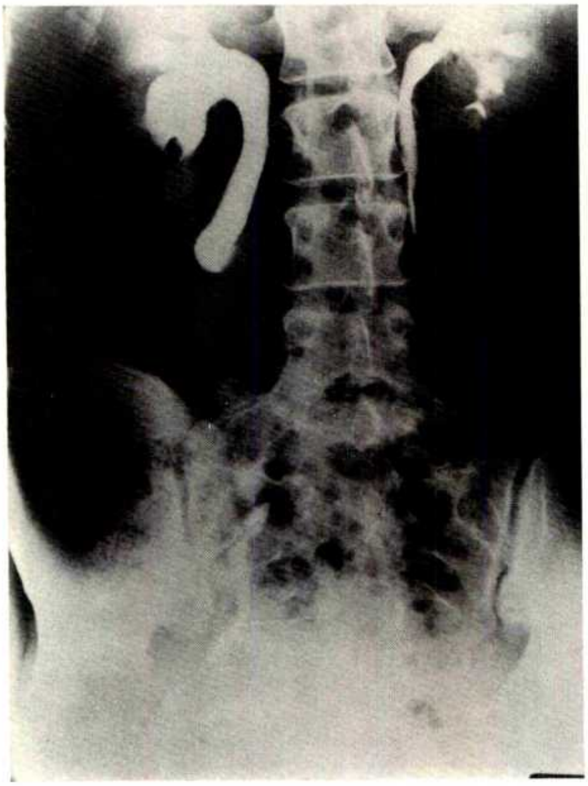


FIG. 1.

Intravenous urogram showing obstruction of right upper ureter.

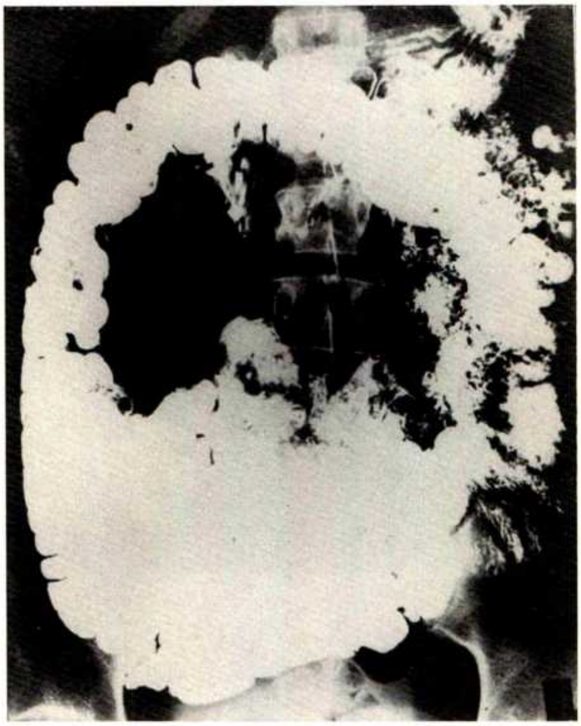


FIG. 2.

Barium follow-through showing upward displacement of hepatic flexure and transverse colon by the mass.

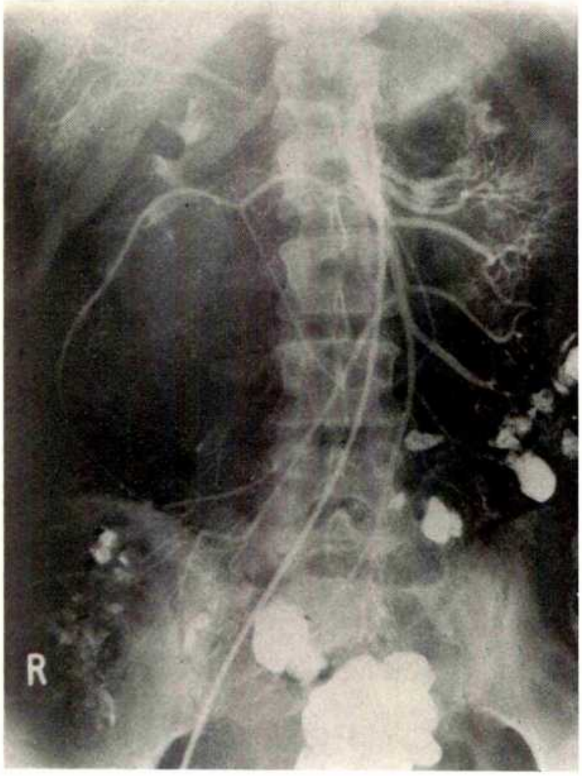


FIG. 3.

Superior mesenteric arteriogram showing displacement of the middle colic artery around the relatively avascular mass.

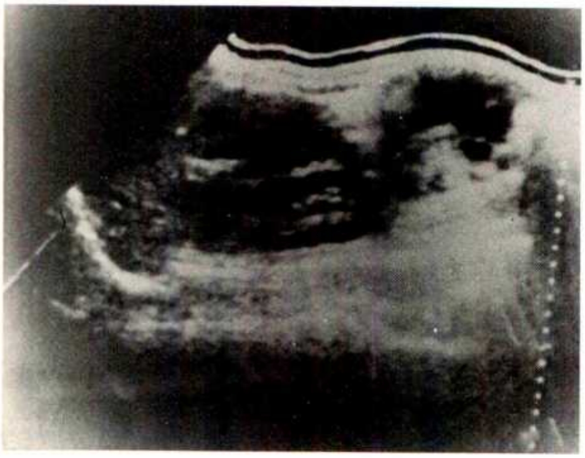


FIG. 4.

Longitudinal scan 6 cm from midline showing a well-defined mass inferior to the liver and gall bladder and antero-inferior to the right kidney. The mass contains both echogenic areas and anechoic rounded structures with posterior echo enhancement consistent with cysts.

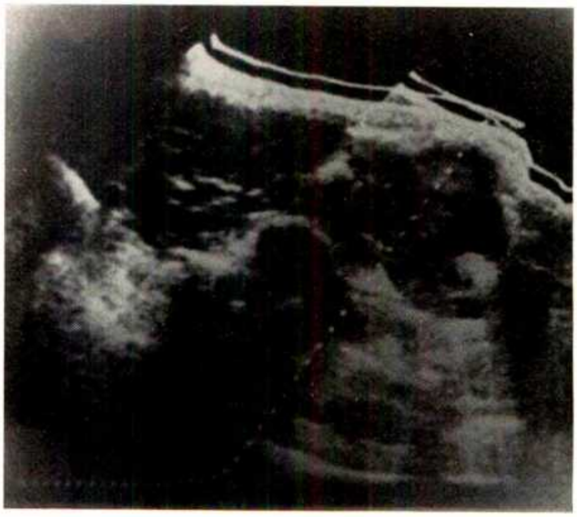


FIG. 5.

Oblique scan through the right kidney and the mass which on this section is chiefly echogenic but with a few anechoic loculi.

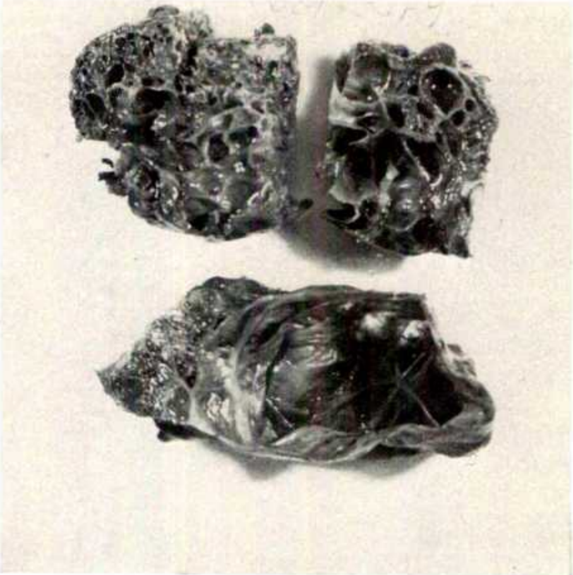


FIG. 6.

Section of specimen which is multilobular and contains numerous loculi of varying size.

At laparotomy, a lobulated dark-red retroperitoneal mass, measuring 17 cm × 12 cm × 6 cm was found in front of and below the right kidney and was excised. Macroscopically, numerous loculi, some filled with brown-coloured fluid and some with solid material were noted (Fig. 6). Microscopically, this was a benign lesion. Large and small ramifying vascular channels with a flattened endothelial lining and external smooth muscle sheaths of variable completeness were present. The interstitial areas contained adipose tissue and lymphoid aggregates. The appearances were those of an angiomatous lymphoid hamartoma (Fig. 7).

1981, *British Journal of Radiology*, *54*, 815–817 SEPTEMBER 1981

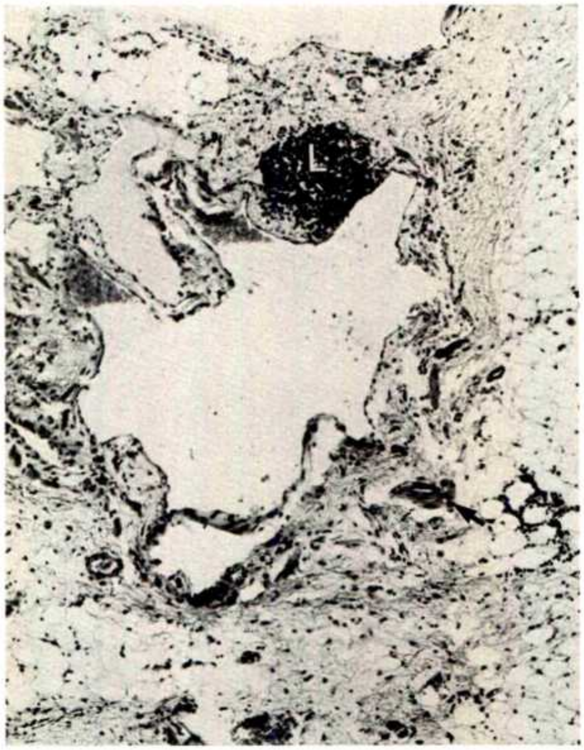


FIG. 7.

Microscopic section showing lymphatic channels with lymphoid tissue (L), adipose tissue and smooth muscle (arrowed) in the walls.

DISCUSSION

Angiomatous lymphoid hamartoma is a benign lesion and is considered to represent either an unusual lymphatic hyperplastic reaction to inflammation or a lymphatic harmartoma (Tung and McCormack, 1967). It occurs most frequently in the thorax, but also in the abdomen and pelvis (Bainbridge, 1976). It presents in early adult life as a mass. The tumour possesses a capsule and is characterised by the presence of lymphoid follicles and a stroma containing vascular channels. Surgical excision is curative.

Previous radiographic findings have included a soft tissue mass, calcification and extrinsic effects on the kidney and ureter. A vascular capsule has been demonstrated at angiography (Tung and McCormack, 1976; Bainbridge, 1976). Pre-operative diagnosis has not been made due to the lack of characteristic radiographic features. In this case ultrasound demonstrated the retroperitoneal position of the mass and adjacent structures. It showed multiple loculi of differing echodensity corresponding to the macroscopic findings.

Retroperitoneal masses have few distinctive features on clinical examination or standard radiological investigations. The contribution of ultrasound in the diagnosis of retroperitoneal masses is that by showing the internal structure of these lesions, it enables some differentiation to be made. It also shows relationships to renal and other retroperitoneal structures. In retroperitoneal sarcoma ultrasound shows a solid lesion with a relatively more echodense central area and no cystic areas (Karp *et al.*, 1980), findings which are quite different from the case described here.

ACKNOWLEDGMENTS

We wish to thank Mr. M. Butler for permission to publish details of this patient under his care and Dr. E. Sweeney for the pathological diagnosis.

REFERENCES

BAINBRIDGE, E. T., 1976. Angiomatous lymphoid hamartoma of the pelvis. *British Journal of Obstetrics and Gynaecology*, *83*, 823–827.

KARP, W., HAFSTRÖM, L. O. and JÖNSSON, P. E., 1980. Retroperitoneal sarcoma. Ultrasonographic and angiographic evaluation. *British Journal of Radiology*, *53*, 525–531.

TUNG, K. S. K. and McCORMACK, L. J., 1967. Angiomatous lymphoid hamartoma. Report of five cases with a review of the literature. *Cancer*, *20*, 525–536.

Ultrasound diagnosis of hydrops fetalis due to fetal tachycardia

By I. M. Shirley, M.B., Ch.B., D.Obst.R.C.O.G., B. A. Richards, M.B., B.S. and R. H. T. Ward, M.A., M.B., B.Chir., M.R.C.O.G.

Departments of Ultrasound and Obstetrics, University College Hospital, London

(*Received February 1981*)

Fetal congestive heart failure due to intra-uterine tachycardia with or without arrhythmia is an unusual cause of hydrops fetalis in the newborn (Silber and Durnin, 1969; Van der Horst, 1970; Etches and Lemons, 1979.) With the increasing use of ultrasound, cases are now being diagnosed during pregnancy (Kerenyi *et al.*, 1980; Rees *et al.*, 1980). We report two further such cases diagnosed *in utero*.

Case Reports

Case 1

A 32-year-old gravida 3, para 1 had an uneventful pregnancy until 34 weeks gestational age, when the uterus was found to be large for dates. The ultrasound scan demonstrated a single live fetus. The bi-parietal diameter (BPD) was 96.3 mm (mean for 38 weeks), and the abdominal circumference (AC) obtained at the level of the liver was 375 mm (360 mm is the mean for term) and there was obvious ascites (Fig. 1). Six days later the AC was 390 mm and there was considerable scalp oedema (Fig. 2). The fetal heart rate was normal and no other fetal abnormality was apparent. The mother's blood group was A Rhesus negative, but no abnormal antibodies were present in her serum. A diagnosis of fetal hydrops of unknown aetiology was made, and a male infant weighing 3760 g with hepatomegaly and ascites was delivered forthwith by caesarean section. Although the fetal heart rate was normal at birth, episodes of regular tachycardia were subsequently noted and treated with digoxin. There was no clinical or echocardiographic evidence of structural cardiac defect, and the infant has subsequently made good progress.

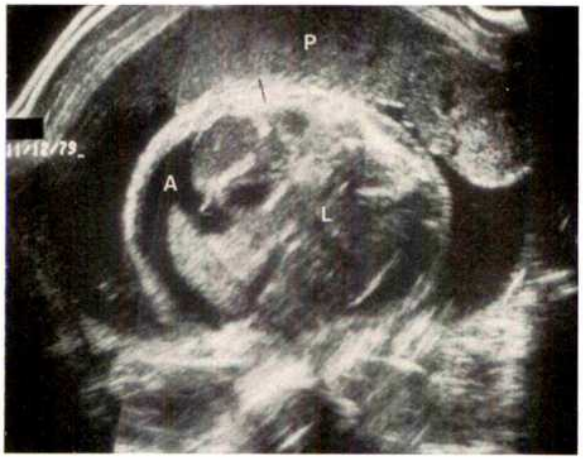


Fig. 1.

Scan showing transverse section of fetal abdomen at level of umbilical vein. L = fetal liver, A = ascites, P = placenta.

Case 2

A 37-year-old primigravida with a history of infertility for 16 years was first seen at approximately 12 weeks gestation. She declined ultrasound examination, maternal serum alphafetoprotein (AFP) estimation and amniocentesis to exclude Down's syndrome in the fetus. Later she agreed to an ultrasound scan, which confirmed the gestational age as 25 weeks (BPD of 67.3 mm and AC of 220 mm) and revealed fetal tachycardia. At 29 weeks the patient was admitted following the sudden onset of oedema of the legs and abdominal wall and an increase in abdominal girth, thought to be due to polyhydramnios. Her blood pressure and urinalysis were normal, and no abnormal antibodies were present in her serum. Ultrasound demonstrated hydrops fetalis, considerable scalp oedema and an abnormally thick anterior placenta (Fig. 3). The BPD was 73 mm (mean for 27–28 weeks) and the AC 350 mm (mean for 39 weeks). The fetal heart rate was rapid, irregular and uncountable. The fetal liver and kidneys appeared normal. Polyhydramnios was not confirmed.

Based on our experience of Case 1, a diagnosis of hydrops due to fetal congestive cardiac failure associated with tachyarrhythmia was made. An intra-uterine electrocardiogram (ECG) and more detailed ultrasound of cardiac structures (Professor S. Campbell) revealed no cardiac abnormalities. Amniocentesis showed a normal amniotic fluid AFP but an immature lecithin sphingomyelin ratio, which is associated with a high incidence of respiratory distress syndrome. Since the fetus was so premature, intra-uterine therapy had to be considered. The maternal ECG and serum electrolytes being normal, the mother was given digoxin 0.25 mg six-hourly for 24 h and thereafter 0.25 mg 12-hourly. The fetal heart rate and AC decreased to 160/min and 300 mm respectively over 72 h. At 30 weeks labour started spontaneously and caesarean section was performed. The grossly oedematous male infant weighed 3350 g and showed considerable generalized oedema. During resuscitation 400 ml of ascitic fluid were aspirated. The placenta weighed 1440 g. ECG showed supraventricular tachycardia (with a 2:1 block and rates up to 440/min) which was successfully controlled at between 130 and 150 beats/min with

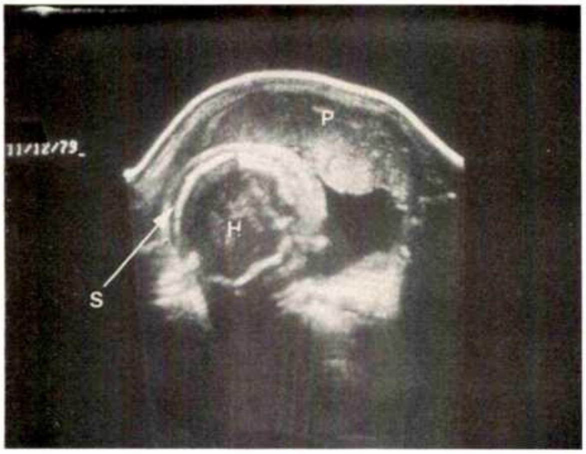


Fig. 2.

Section of fetal head showing double line of scalp oedema (S), H = head, P = placenta.

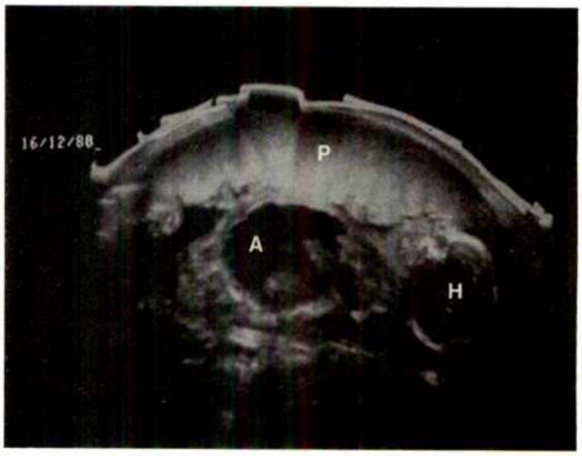


Fig. 3.

Longitudinal section of fetus showing massive ascites and a thick placenta. A = ascites, H = head, P = placenta.

1981, *British Journal of Radiology*, *54*, 817–818

SEPTEMBER 1981

digoxin therapy. Progress was satisfactory until the fourth day when unexplained circulatory failure occurred and supportive therapy was discontinued. The body weight at post-mortem was 1535 g. No cardiac or other abnormality was noted, but there was antemortem thrombus in the left atrium, left ventricle and ascending aorta.

DISCUSSION

The ultrasound diagnosis of fetal hydrops depends on the demonstration of fetal ascites (Figs. 1 and 3), a larger abdominal circumference than normal for dates and subcutaneous and scalp oedema, sometimes with polyhydramnios and placental enlargement.

In neither of these cases was fetal ascites suspected prior to ultrasound examination. Subsequent management was influenced by the serial measurements of the AC and fetal heart rate, an assessment which may be more accurate than cardiotocography (Rees *et al.*, 1980). In the first case, the oedema increased, whereas in the second case, despite an inadequate (in retrospect) maintenance dose of digoxin, the fetal cardiac failure improved. The finding of fetal tachycardia at ultrasound examination should raise the possibility of incipient fetal cardiac failure, as early therapy *in utero* can now be safely considered before premature delivery (Kerenyi *et al.*, 1980).

ACKNOWLEDGMENTS

We thank Professor H. A. Brant for his permission to include details of a patient under his care, and Professor Stuart Campbell for his expertise.

REFERENCES

ETCHES, P. C. and LEMONS, J. A., 1979. Non-immune hydrops foetalis: Report of 22 cases including three siblings. *Paediatrics*, *64*, 326–332.

KERENYI, T. D., GLEICHER, N., MELLER, J., BROWN, E., STEINFELD, L., CHITKARA, U. and RAUCHER, H., 1980. Transplacental cardioversion of intra-uterine supraventricular tachycardia with digitalis. *Lancet*, *ii*, 393–394.

REES, L., VLIES, P. R. and ADAMS, J., 1980. Hydrops fetalis, an unusual cause, presentation and method of diagnosis. *British Journal of Obstetrics and Gynaecology*, *87*, 1169–1170.

SILBER, D. L. and DURNIN, R. E., 1969. Intrauterine atrial tachycardia associated with massive oedema in a newborn. *American Journal of Diseases of Children*, *117*, 722–726.

VAN DER HORST, R. L., 1970. Congenital atrial flutter and cardiac failure presenting as hydrops foetalis at birth. *South African Medical Journal*, *44*, 1037–1039.

Triple gall bladder

By D. R. Foster, D.M.R.D., F.R.C.R.

Department of Diagnostic Radiology, Royal Perth Hospital, Wellington Street, Perth, Western Australia

(*Received February 1981*)

Triple gall bladder is a rare congenital anomaly. It was first reported separately in 1958 by Boni and by Skielboe. Since then only four further cases have appeared in the literature. An additional case demonstrated on routine oral cholecystography is described, together with a review of the literature.

CASE REPORT

A 46-year-old male complaining of right hypochondrial pain was investigated by oral cholecystography. Physical examination was unremarkable.

A cholecystogram with tomography (Fig. 1) demonstrated three separate gall bladders. There were calculi present in one of the gall bladders which drained directly into the common duct, via a single cystic duct. The cystic ducts of the other two gall bladders fused prior to insertion into the common bile duct.

DISCUSSION

There are three types of triple gall bladder, depending on the number of cystic ducts and their insertion into the common bile duct (Fig. 2).

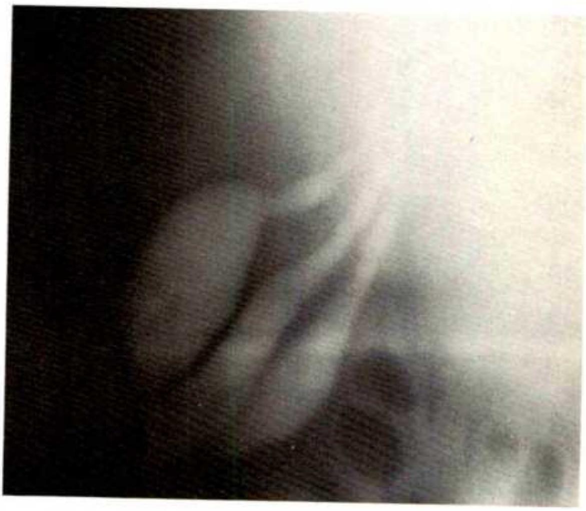


FIG. 1.

Tomogram (after fatty meal study) demonstrating triple gall bladder; one contains calculi.

(a) Three cystic ducts form one common cystic duct before entering the common duct.

(b) Two cystic ducts join before entering the common duct whilst the third cystic duct joins the common duct separately.

(c) All three cystic ducts empty separately into the common duct.

Boyden (1926) presented the classic study of double and triple gall bladders. He studied 10,000 domestic animals, recording 456 duplications and 20 triplications of the gall bladder. He also reported a cadaver series of 9,220 and a radiographic series of 9,770 in man. There were two cadaveric and three radiographic cases of duplication but no case of triple gall bladder. Embryologically, he postulated that multiple gall bladders represented an outgrowth of a secondary vesicle from some other portion of the biliary duct system subsequent to the formation of the definitive gall bladder. In the human embryo, small cellular outpouchings called rudimentary bile duct buds occur at the junction of the hepatic ducts. These duct buds usually regress and disappear but if they persist, they may represent the aetiology of double or triple gall bladder.

In 1958 Skielboe and Boni each described triple gall bladders. In both cases three cystic ducts entered the common duct separately. Skielboe's case was demonstrated on cholecystography, although the presence of the third gall bladder was only recognised retrospectively, following surgery. All three gall bladders contained calculi.

In 1959 Kelley and Hause both reported triple gall bladders diagnosed radiologically and pathologically respectively. Carls (1963) described a case identical to the present one, with three separate cystic ducts, two of which joined before entering the common duct.

Ross and Sachs (1968) noted that in their case intravenous cholangiography and tomography aided definition of the gall bladders and duct systems. It is interesting to observe that, except for this case, at least one of the three gall bladders has always contained calculi.

ACKNOWLEDGMENT

I wish to acknowledge the late Dr. A. A. Merritt, who was responsible for the care of this patient.

REFERENCES

BONI, R., 1958. Cistifellea tripla and bile calcarea. *Radiologia Medica.*, *44*, 833–844.

BOYDEN, E. A., 1926. Accessory gall bladder; embryological and comparative study of aberrant biliary vesicles, occurring in man and domestic mammals. *American Journal of Anatomy*, *38*, 177–231.

CARLS, P., 1963. Triplication and other anomalies of gall bladder with report of case. *Millard Gillmore Hospital Bulletin*, *10*, 73–78.

HAUSE, W. A., 1959. Triplication of gall bladder. *A.M.A. Archives of Surgery (Chicago)*, *79*, 144–145.

KELLEY, A. R., 1959. Triple gall bladder: a case of double gall bladder with associated anomalous gall bladder. *Medical Journal of Australia*, *46*, 124–126.

ROSS, R. J. and SACHS, M. D., 1968. Triplication of the gall bladder. *American Journal of Roentgenology*, *104*, 656–661.

SKIELBOE, B., 1958. Anomalies of gall bladder: vesica fellae triplex: report of a case. *American Journal of Clinical Pathology*, *30*, 252–255.

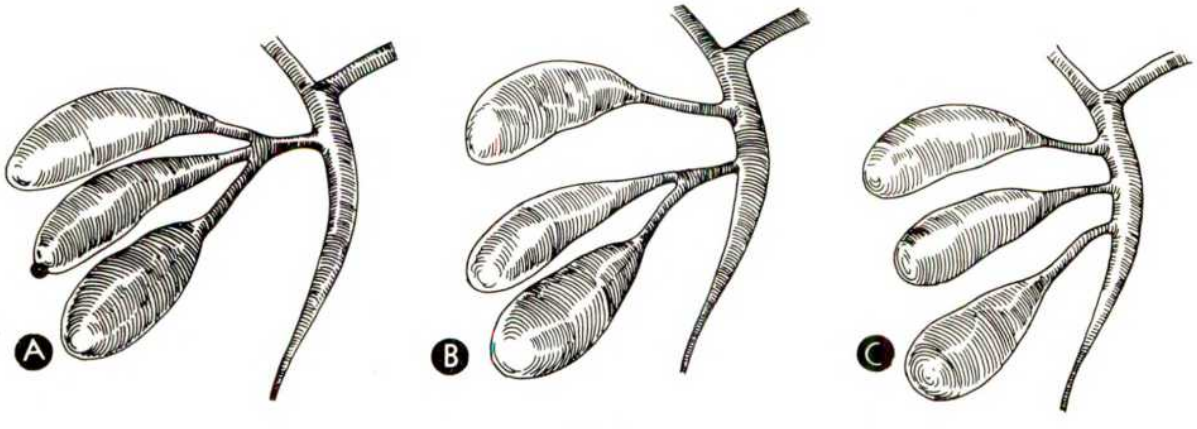


FIG. 2.
Anatomical variations of triple gall bladder.

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Léri's pleonosteosis

THE EDITOR—SIR,

Since the submission of our paper, a study of a kindred with Léri's pleonosteosis has been published (Hilton and Wentzel, 1980) and we have had a further opportunity to review Case 1.

Shortening and broadening of the metacarpals, metatarsals and phalanges with flexion deformities were confirmed as important features in young patients. In addition a relative decrease in AP diameter of the vertebral bodies of L2 and L3 was seen in an eight year old boy. Our Case 1 has shown some developmental arrest and also shows now mild hypoplasia of the body of L1.

It is interesting to speculate that these cases are in reality mild mucolipidoses without the more usual severe osseous changes of mucolipidosis III and the less severe manifestations would be very consistent with a dominant rather than a recessive inheritance in some reported cases. Further fibroblast studies would be interesting.

Yours etc.,
D. G. SHAW.

Queen Elizabeth Hospital for Children,
Hackney Road,
London E2 8PS.

(Received June 1981)

REFERENCES

FRIEDMAN, M., LAWRENCE, B. M. and SHAW, D. G., 1980. Léri's pleonosteosis. *British Journal of Radiology*, *54*, 517–518.

HILTON, R. C. and WENTZEL, J., 1980. Léri's pleonosteosis. *Quarterly Journal of Medicine*, *49*, 419–429.

Ultrasound in hepatoma

THE EDITOR—SIR,

Dubbins *et al.* (1981) state that the echo pattern provides little help in the differentiation of primary from secondary carcinoma. Their finding of an echo-free pattern in 47% of cases is at variance with the findings of Boultbee (1979) who described echogenic lesions in 67% of cases and mixed lesions in 27%.

My own experience (Calder *et al.*, 1980; De Cock and Calder, 1981) of ultrasound in 18 Kenyan Africans with subsequently proven hepatoma showed that all of these tumours contained at least some echogenic areas. I agree with Boultbee that, in African patients, the ultrasonic demonstration of a large irregular echogenic space-occupying lesion with irregular margins indicates the possibility of hepatocellular carcinoma. I should be reluctant to diagnose hepatoma in an African patient in the absence of at least some strong echoes within a hepatic mass. This apparent difference in echo characteristics between African and European patients might be explained, at least in part, by the generally late presentation and advanced state of the disease in the former.

Yours, etc.,
J. F. CALDER.

Department of Diagnostic Radiology,
Aberdeen Royal Infirmary,
Foresterhill,
Aberdeen AB9 2ZB.

REFERENCES

BOULTBEE, J. E., 1979. Grey scale ultrasound appearances in hepatocellular carcinoma. *Clinical Radiology*, *30*, 547–552.

CALDER, J. F., DE COCK, K. and STASS, B., 1980. Diagnostic ultrasound in abdominal disease—first experiences in Kenya. *East African Medical Journal*, *57*, 607–614.

DE COCK, K. and CALDER, J. F., 1981. The use of ultrasound in tropical abdominal disease. *Transactions of the Royal Society of Tropical Medicine and Hygiene* (in press).

DUBBINS, P. A., O'RIORDAN, D. and MELIA, W. M., 1981. Ultrasound in hepatoma—can specific diagnosis be made? *British Journal of Radiology*, *54*, 307–311.

Mullard 4 MV linear accelerator at Newcastle upon Tyne

THE EDITOR—SIR,

Some of your readers may be interested to know that the Mullard 4 MV linear accelerator installed at Newcastle General Hospital in 1953 has now been withdrawn from service. The machine was among the very first linear accelerators to be designed specifically for clinical radiotherapy and it represented a major step forward in high-energy technique, owing much to the foresight of Mr. C. J. L. Thurgar, director of radiotherapy and Dr. F. T. Farmer, who was in charge of the physics team. As well as having the well-known physical advantages of high particle energy, the accelerator produced dose-rates high enough to enable large numbers of patients to be treated. Moreover, the accelerator was gantry-mounted with fully isocentric movements, closely following the ideas of Howard-Flanders and Newbery (1950), although it was not until several years later that the term "isocentre" was coined by Boland.

Commissioning of the accelerator commenced on site on August 8, 1953, when the output at 1 m was estimated as 120 r/min, based on measurements made using condenser-chambers calibrated with a standard radium source. The field-flatness checks were completed in September and a quadrant chamber to monitor the polar diagram was installed in October. The first depth-dose curve was measured in November—the percentage depth-dose for a 10×10 cm field was 61% at 10 cm depth. Systematic depth-dose measurements, including the build-up region, occupied most of December. A number of improvements giving increased and more stable output (200–250 r/min) and larger field size were later introduced, though the basic design remained unaltered (Day and Farmer, 1958).

The first treatment was carried out on December 3, 1953 and the last treatment was completed on May 22, 1981. The statistics of clinical usage indicate that altogether 18272 courses of treatment were given, involving 297852 attendances of patients and the application of well over 600000 separate treatment fields.

We felt it would be useful to record these basic facts as a footnote to the history of high-energy radiotherapy.

Yours, etc.,
W. M. ROSS,
M. J. DAY.

Newcastle General Hospital,
Newcastle upon Tyne NE4 6BE.

(Received June 1981)

REFERENCES

DAY, M. J. and FARMER, F. T., 1958. The 4 MeV linear accelerator at Newcastle upon Tyne. *British Journal of Radiology*, *31*, 669–682.

HOWARD-FLANDERS, P. and NEWBERY, G. R., 1950. The gantry type of mounting for high voltage X-ray therapy equipment. *British Journal of Radiology*, *23*, 355–357.

1981, *British Journal of Radiology*, *54*, 820

Correspondence

X-ray tube lifetime and image quality in computed tomography

THE EDITOR—SIR,

In a recent communication Shrimpton and Dewhirst (1981) rightly imply that an effective method of reducing CT scanner "down time" during installation of X-ray tubes is to minimize the frequency with which tubes are renewed. They further assert that it is cost-effective to extract the maximum possible lifetime from an X-ray tube. The truth of this statement appears self-evident only if no account is taken of the financial method of charging for replacement tubes adopted by EMI Medical, and continued by IGENY, to which most users in the United Kingdom are subject. This involves levying a standard price for a new tube "guaranteed" to yield 500 hours' use. However, the price is reduced by a *pro-rata* rebate for hours less than 500 actually obtained from the previous tube. Thus, no financial benefit accrues to the purchaser by prolonging tube use until after 500 hours has been achieved. Since Dewhirst and Shrimpton quote the figure of 300 hours average tube life for an EMI CT1010 head scanner, and a similar figure applies to the EMI CT5005 whole body scanner, it is clear that tube lifetime in excess of 500 hours is the exception rather than the rule.

Hence, within the limit of 500 hours the diagnostic quality of the image is the only consideration relevant to a decision on tube renewal, save that of avoiding unnecessary down time. If image quality is deteriorating and a stage is reached at which the user and the tube supplier are agreed on the desirability of replacing the X-ray tube, there is no financial benefit in delaying.

Shrimpton and Dewhirst also state that in Leeds, "... continued running of the tubes outside the EMI factory tolerance has not unduly compromized the diagnostic capability of the machine, whilst allowing maximum utilization of the tubes". One inference to be drawn from this is that patients are normally subjected to somewhat greater radiation exposure than is absolutely necessary—a practice of which all users may at times be guilty. If tubes were operated with tube current at the minimum level required, this only being increased in order to compensate for declining output, then not only would less dose be received by the patient but in all probability tube lifetime would be further prolonged.

Yours etc.,
C. B. SMITH.

West of Scotland Health Boards,
Department of Clinical Physics and Bio-engineering,
11 West Graham Street,
Glasgow G4 9LF.

(*Received March 1981*)

REFERENCE

SHRIMPTON, P. C. and DEWHIRST, D. W., 1981. X-ray tube lifetimes with the Leeds General Infirmary EMI brain scanner. *British Journal of Radiology*, *54*, 157–158.

(*Authors' reply*)

THE EDITOR—SIR,

We would like to make the following points in response to Dr. Smith's letter.

1. The main conclusion of our communication was that the local operating conditions employed at the Leeds General Infirmary appeared to result in X-ray tube lifetimes significantly above the apparent national average for CT1010 brain scanners. We believe maximum utilization of X-ray tubes to be cost-effective under our circumstances.

2. The replacement of X-ray tubes has continued to be a thorny problem since the introduction of the EMI scanner. The manufacturer's policy on tube cover has recently undergone a major revision, and other such changes may occur in the future.

3. The minimization of dose to the patient commensurate with adequate diagnosis is fundamental to radiation protection. Dr. Smith rightly refers to the change in dose which occurs with declining output of an aging X-ray tube, something of the order of 15%. However, with regard to over-exposure of patients, it is worth noting that use of the special high-accuracy, high-resolution modes for scanners can result in doses which are five times larger than those for normal scans (Wall *et al.*, 1979). The clinical justification of all CT scans, especially those involving slow scanning speeds, is clearly of prime importance for the protection of the patient.

Yours etc.,
*P. C. SHRIMPTON,
D. W. DEWHIRST.

The University of Leeds,
Department of Medical Physics,
The General Infirmary,
Leeds LS1 3EX.

(*Received June 1981*)

REFERENCES

SHRIMPTON, P. C. and DEWHIRST, D. W., 1981. X-ray tube lifetimes with the Leeds General Infirmary EMI brain scanner. *British Journal of Radiology*, *54*, 157–158.
WALL, B. F., GREEN, D. A. C. and VEERAPPAN, R., 1979. The radiation dose to patients from EMI brain and body scanners. *British Journal of Radiology*, *52*, 189–196.

---

*Present address: NRPB, Chilton, Oxon.

Hybrid real time/B scan ultrasonic system

THE EDITOR—SIR,

We were interested to read the technical note by Wild *et al.* (1981). We have used a similar system and agree wholeheartedly with the majority of their observations. We feel, however, that linear array real time systems have a valuable role in obstetric scanning.

The sector scanner is particularly valuable in obstetrics in the examination of early pregnancies because the scanning action allows the beam to be more or less normal to the vagina, cervix and body of the uterus giving excellent images and in later pregnancy this type of scanning action is important in showing the cervix and lower segment in cases of suspected placenta praevia. However, in later pregnancy the field of view is more restricted than that of linear array scanners and it is more difficult to be certain of the orientation of the beam. We have not found the rotating probe sector scanner interfaced to our Diasonograph as easy to use for cephalometry as the linear array of our ADR fitted with Kretz bar calipers and suspect that measurements made with it are subject to a greater random error than those made using a linear array or a B scan method (Davies, 1980). Work is in progress to assess this hypothesis.

There are two problems with rotating probe scanners for cephalometry using dynamic methods.

1. It is difficult to assess when the beam is normal to the mid-line.

2. It is difficult to know and to control the orientation of the probe so that a maximum diameter is measured.

We feel that dynamic methods are superior to static methods of cephalometry and that a linear array real time machine with bar calipers is the method of choice for cephalometry (Davies and Richardson, 1979).

We entirely agree with Wild *et al.* (1981) that a hybrid scanner as described is desirable, but we think that the addition of a high quality linear array greatly improves the diagnostic capabilities of the machine.

Yours etc.,
R. E. RICHARDSON,
P. DAVIES,

Departments of Radiology and Medical Physics,
City Hospital,
Hucknall Road,
Nottingham NG5 1PB.

(*Received April 1981*)

REFERENCES

WILD, S. R., COPLAND, W. A. and McDICKEN, W. N., 1981. A hybrid real time/B scan ultrasonic system. Implications for clinical practice based on a two year experience. *British Journal of Radiology*, *54*, 356–358.

DAVIES, P., 1980. Ultrasonic fetal cephalometry and its errors, the value of iterative and dynamic methods. D.M. thesis. University of Nottingham.

DAVIES, P. and RICHARDSON, R. E., 1979. Dynamic fetal cephalometry. *British Journal of Obstetrics and Gynaecology*, *86*, 765–772.

(*Authors' reply*)

THE EDITOR—SIR,

We are pleased to know that the experience of Drs. Davies and Richardson with a hybrid system is in general similar to our own. Our main concern was with the success of the system in upper abdominal work but we should like to comment on their remarks concerning real time scanning in obstetrics. Undoubtedly the sector scanner is superior to the linear array in early pregnancies and we have not encountered any serious problems with its use in later pregnancy. The field of view in later pregnancy need not necessarily be limited if the 180° sector option is employed. Indeed we have found that it is often difficult to use the full length of a linear array when the abdomen is very convex in late pregnancy.

We would agree that the Kretz bar calipers are easier to use than the radial calipers of the sector scanner, but feel that the ideal system would incorporate omnidirectional calipers. We also feel that dynamic methods of cephalometry are superior to B scanning. We have, however, not experienced any particular difficulty in controlling orientation of the sector scan probe but look forward with interest to Dr. Davies's results in assessing comparative errors of sector scanners, B scanners, and linear arrays in cephalometry.

Yours, etc.,
S. R. WILD,
W. N. McDICKEN.

Departments of Radiology,
and Medical Physics, Western General Hospital
Royal Infirmary, Edinburgh.

(*Received May 1981*)

REFERENCE

WILD, S. R., COPLAND, W. A. and McDICKEN, W. N., 1981. A hybrid real time/B scan ultrasonic system. Implications for clinical practice based on a two year-experience. *British Journal of Radiology*, *54*, 356–358.

Book review

Uroradiology. By Thomas Sherwood, Alan J. Davidson and Lee B. Tanner, pp. viii+351, 1980 (Blackwell, Oxford, London, Edinburgh, Melbourne), £35·00.
ISBN 0-632-00493-Z

"The solution to every radiological problem lies in another film". The difficulties inherent in this maxim are how and when should the appropriate film be obtained. Nowhere is this potentially greater than in the selection of the most helpful investigation for the evaluation of urinary-tract disease. The modern radiologist has at his disposal an ever-increasing variety of techniques, each of which continues to develop in sophistication, application and accuracy. Too often these methods are viewed as mutually competitive, so obscuring their important complementary nature. It has also become fashionable to employ too many in rigid investigation protocols.

In this new book, Professor Thomas Sherwood has successfully produced both a comprehensive and a comprehensible guide through the maze of urinary-tract investigations which are discussed in terms of their relevance to presenting clinical problems. The importance of close collaboration between referring clinician and investigating radiologist is given proper emphasis. The script is full of sound common sense and the clear presentation will enthuse the reader as well as inform. The illustrations have been well chosen and are, on the whole, beautifully reproduced. The references appended to each section have obviously been very carefully selected and provide a most satisfactory guide to further reading.

It is impossible to resist the author's invitation to indulge in semantic quibbles and assert that medullary sponge kidney should be excluded from the general diagnosis of nephrocalcinosis from which it is readily distinguished. Similarly one might regret the perpetuation of the myth that sarcoidosis is a cause of nephrocalcinosis based on but two cases in the literature. Calcification in the wall of a simple cyst, much beloved by American authors, is illustrated but happily the author reveals his true feelings by appending the words "autopsy proof" to the accompanying legend. Excretion urography has been denigrated as inaccurate in the diagnosis of renal cell carcinoma. Experience shows that a meticulous attention to technique and a careful evaluation of signs will with practice achieve an accuracy at least comparable with that of ultrasound and CT. This accuracy is of great importance in facilitating the selection of further investigation and in the identification of other causes of superficially similar lesions. The time has surely come for the IVU to be rediscovered as the most valuable tool in the diagnosis of renal masses.

Enough of this quibbling! The presentation of a subject with clarity and brevity always affords scope for disagreement on matters of detail. This book is a significant addition to the radiological literature. It stimulates and facilitates further study of the subject in depth and enables all that is learnt to be placed in perspective. Clearly it must be included in the libraries of all teaching units of radiology and urology. It will prove invaluable as a bench book in all radiological departments, but will, however, pose the perennial problem of how to combine its availability with adequate security.

J. ROYLANCE.

1981, *British Journal of Radiology*, 54, 822–824

Proceedings of The British Institute of Radiology

Radiographic systems: what is best?

Abstracts of papers presented at a meeting held on Wednesday, March 18, 1981 at The Reid-Knox Hall, 32 Welbeck Street, London W1M 7PG

Introduction—the nature and purpose of radiological investigations, by J. Roylance.
The physical basis for characterization of radiographic images, by R. E. Stapleton.
The influence of focal spot size in image quality, by G. Waters.
The performance of the image receptor with special reference to film-screen combinations, by B. M. Moores.
Methods for achievement of minimum doses, by J. H. E. Carmichael.
Some aspects of radiographic technique: (i) the advantages of air gaps in dose reduction; (ii) the influence of inevitable patient movement, by G. M. Ardran.
An assessment of intravenous urography imaging using 100 mm and conventional films, by Elizabeth M. Robertson, B. Baily, Tamarisk M. Hearnden, R. F. Mould and D. H. Trapnell.

THE NATURE AND PURPOSE OF RADIOLOGICAL INVESTIGATIONS

By J. Roylance

Bristol Royal Infirmary, Bristol

The role of radiology within the wide variety of disciplines involved in patient care, and the relative values of the increasing number of investigative techniques available for patient care were discussed with particular reference to diseases of the urinary tract. The concept of the definitive diagnostic test was presented and the ways in which the level of confidence in a particular diagnosis may be increased were illustrated with examples of simple renal cyst and renal cell carcinoma. The management role of radiology was also reviewed, with emphasis on the determination of the precise stage of the disease and the developing application of interventional radiology to therapy.

It was argued that the final assessment of the merits of radiographic systems must rest on the benefit which accrues to patients. Attention was paid to the conflicting demands for simple designs enabling flexible application, and the needs of sophisticated equipment for specialized procedures. The conflicting factors involved in the production of images with consistent high definition and contrast were also of great relevance.

Radiographic systems should be subjected to a simplistic cost-benefit analysis. The costs include:

1. Intrinsic hazards arising from radiation, those associated with the special investigations and the risks of inaccurate diagnosis; these can be reduced by suitable equipment design, but also require high expertise in both radiography and interpretation.
2. Capital funds required for the purchase of equipment and the space required for installation; these demand simple, flexible and durable design.
3. Revenue which is used for staff, materials and maintenance; these are influenced by the systems used and the patient throughput.

THE PHYSICAL BASIS FOR CHARACTERIZATION OF RADIOGRAPHIC IMAGES

By R. E. Stapleton

Ilford Ltd., Brentwood, Middlesex

Radiographic image quality is characterized by sharpness, noise and photographic contrast. Sharpness is measured objectively as a Modulation Transfer Function (MTF), but this needs to be multiplied by the contrast and by the eye's frequency response to obtain the subjective sharpness.

The MTF of a radiograph depends on the screen, focal spot size, magnification, and subject movement. All these factors can be expressed in terms of their MTF's. Optimum sharpness is achieved when these are equal. Excess sharpness in any factor should be "traded off" to improve the least sharp component. Magnification can be used to adjust the effective screen sharpness with respect to the subject plane.

In fast systems the noise is mainly quantum mottle, caused by the random distribution of X-ray photons amplified by high conversion efficiency. It is inevitably related to the square root of the speed of the film/screen system for a given phosphor absorption, but it is modified by the system sharpness and also by contrast. Again, magnification can be used to reduce the effective noise with respect to the subject.

The optimum combination of sharpness and noise varies with the size and contrast of the subject detail and with viewing conditions.

Subjects with fine, high-contrast detail may be sharpness-limited, and the system is then easily adjusted for optimum quality. More generally, the important detail has involved both lower frequency and lower contrast and is noise-limited—it is then more difficult to determine the optimum. A slow film/screen system used with somewhat unsharp geometry may give the best diagnostic quality.

THE INFLUENCE OF FOCAL SPOT SIZE IN IMAGE QUALITY

By G. Waters

Machlett X-ray Tubes (G.B.) Ltd., Wembley, Middlesex

The imaging quality of the focal spot of an X-ray tube is dependent not only on its size; the distribution of the X-ray emission within the spot makes a significant contribution to the final result. Particularly with the modern rotating anode X-ray tube, factors other than the area of the focal spot, e.g. rotational speed, target angle, etc., make a substantial contribution to its electrical power rating and hence its ability to freeze motion in the subject under examination.

It is insufficiently appreciated that focal spots change their imaging characteristics with different electrical loadings as a result of consequent alterations both in dimensions and X-ray emission distribution. From the very nature of the "line focus" there is a unique imaging characteristic for every point in the image plane. In these circumstances it can be argued that excessive attention is paid to the focal spot characteristic on the central ray and under a limited range of electrical loadings.

There is no simple method of describing or measuring the imaging performance of a focal spot, even on the central ray or at a particular electrical loading. It is suggested that a "limiting resolution" technique using a star pattern represents a useful compromise between the determination of the complete Modulation Transfer Function, and the uncertain meaning of the focal spot dimensions as measured with a pinhole technique. It must be pointed out that the star pattern is not a method of measuring focal spot size.

Similarly, there is no simple answer to the question "What is best?". In selecting an X-ray tube for a particular examination, whilst consideration must be given to its imaging characteristics, these must be taken in conjunction with the geometry and performance of other components in the imaging chain, and related to the characteristics of the subject being imaged—area, detail size, rate of movement, contrast etc. With this information and other imposed constraints it should be possible to effect a compromise that will provide an answer to "What is best in the circumstances?"

THE PERFORMANCE OF THE IMAGE RECEPTOR WITH SPECIAL REFERENCE TO FILM-SCREEN COMBINATIONS

By B. M. Moores

Regional Department of Medical Physics,
Christie Hospital, Manchester

It is estimated that there are over 60 000 tungstate and 8000 rare-earth based pairs of intensifying screens in use in England and Wales. The screens with their associated film are produced by 5–10 major manufacturers and there are an enormous number of possible film/screen combinations.

The inability of the user clearly to rationalize the choices of systems available is in no small measure due to historical categorization of film/screen combinations according to speed. This viewpoint arises from two main considerations:

1. Film/screen speed in isolation from final image quality is meaningless. Imaging systems with similar speeds under identical radiographic conditions can, and do, have wide variations in image quality.
2. The definition of speed in terms of exposure necessary to produce a given film density is impractical. It need bear no relation to the number of X-ray photons actually contributing to the final image, particularly when considering the wide range of X-ray beam qualities involved in radiological practice.

The structural properties of film/screen combinations dictate the final imaging performance, and realistic systems are obviously a compromise between several competing requirements. It should be possible, however, to categorize film/screen combinations according to their imaging performance and then relate this to the radiation exposure. Easily measured and physically useful image quality parameters are:

(a) High-contrast limiting resolution.

(b) Large-area low-contrast detectability at a particular film density and under specified radiographic and viewing conditions.

(c) The exposure necessary to produce a given film density.

(d) The contrast detail diagram under specified radiographic and viewing conditions.

This type of approach is already being applied to fluoroscopic imaging systems and CT scanners and, if applied to radiographic systems, would lead to a coherent framework for assessing the dose-efficiency of all radiological imaging systems.

METHODS FOR ACHIEVEMENT OF MINIMUM DOSES

By J. H. E. Carmichael

Broadgreen Hospital, Liverpool L14 3LB

The need for minimum dosage arises from the desire to fulfil the aim of radiation protection that every dose should be as low as is reasonably achievable. In radiography three technical factors influence the performance—the film/screen combination, the processor, and the generator. Film variation can be ignored. A decision should be made by every department as to whether rare earth screens are acceptable for general usage. If used the cost is covered in three years, as the matching film is 6% cheaper, being of lower silver content. Processors should be the most reliable piece of apparatus in the chain, provided test strips exposed on a sensitometer are used.

Generators can be shown to be very variable in output. It may be very difficult to achieve comparability between two apparently similar generators in a department, causing difficulty for staff moving from one to the other. Simple testing of the generator output will also show that any one generator itself may vary. Acceptable limits of variation were suggested—not more than 5 kV difference between weekly testing and not more than 5 kV variation from a mean over a period of three months. A survey of 21 generators showed that only half fell into the limits of acceptability; single-phase generators were considerably more reliable than three-phase.

Reject analysis surveys show that when using automatic exposure control in radiography, there may still be an unacceptably high rate of rejection from exposure causes—possibly higher than manual control. Use of a phantom in mammography will show which technique gives the highest information at the lowest radiation dose, taking into account the target and the recording medium. In fluoroscopy the high doses received during automatic brightness control were stressed. Testing with a phantom by physicist or engineer will show if an intensifier chain is functioning correctly. The relative doses from use of conventional film and 100 mm camera depend on the use or otherwise of rare earth screens. Finally, the detriment of radiological activities in respect of the production of radiation-induced cancer was discussed.

SOME ASPECTS OF RADIOGRAPHIC TECHNIQUE:
1. THE ADVANTAGES OF AIR GAPS IN DOSE REDUCTION; 2. THE INFLUENCE OF INEVITABLE PATIENT MOVEMENT

By G. M. Ardran

University Department of Radiology,
Radcliffe Infirmary, Oxford OX2 6HE

The aim of a radiological examination should be to obtain as much information as possible with the minimum expenditure of time, effort and materials and with the smallest practicable radiation dose.

The use of an air gap instead of an anti-scatter grid will reduce the patient dose by factors of two to five. Air gaps have been used for the chest, cervical spine, surveys for scoliosis, lateral pelvimetry, follow-up congenital dislocation of the hips, mammography and in practically all examples of macroradiography. The degree of effective reduction in scatter will depend on the depth of the air gap, usually 15 cm or more, the size and shape of the field, the thickness of the part irradiated and its physical and chemical nature. Of course, factors which affect contrast, such as quality of radiation and gamma of the film and processing conditions are also important. In practice an air gap may be used in many dose-sensitive circumstances, whether one is concerned with the patient or with a fibre optic device.

Blurring due to inevitable movement of the part being radiographed may be effectively lessened by a reduction of the exposure time if this is practicable. The anatomical parts in the region of the pharynx during swallowing may be moving at the rate of 1000 mm/s whereas those in the small bowel may not exceed 100 mm/s. In the large bowel, the movements are much slower, varying between 10 and 250 mm/min. The advancing edge of the contrast medium in blood vessels can easily move at up to 500 to 1500 mm/s. In order to obviate movement blurring, one would need exposures in the fractions of ms. Thus, ideally the shorter the exposure time the better but in practice the shortest time will depend on the contrast and the degree of blurring acceptable, bearing in mind the limitations imposed by the generator and the X-ray tube.

AN ASSESSMENT OF INTRAVENOUS UROGRAPHY IMAGING USING 100 MM AND CONVENTIONAL FILMS

By Elizabeth M. Robertson, B. Baily,
Tamarisk M. Hearnden, R. F. Mould and
D. H. Trapnell

Westminster Hospital, London SW1

A clinical trial was designed to compare the amount of useful diagnostic information obtained from the 10 min film of an IVU when using either indirect (100 mm) or conventional radiography (25 cm × 30 cm). The films for 50 patients were independently examined by ten radiologists. Eight film readers considered conventional radiography to be significantly better, $p < 0.02$, than indirect (100 mm) radiography, and two film readers considered that there was no significant difference. Possible applications of the technique were briefly described.

ECONOMIC CONSIDERATIONS

By R. T. Rogers

DHSS, Scientific and Technical Branch, 14 Russell Square, London WC1B 5EP

The question "What is best?" for a radiographic system cannot be considered in isolation from costs, for example the use of rare-earth screens, 100 mm radiography and silverless imaging.

To replace existing calcium tungstate screens and cassettes with rare-earth screens might cost over £5 million for England and Wales and add £0.5 million to annual replacement costs but patient dose may be halved. Whether the benefit is worth the cost is for others to decide but the number required might be reduced if their use could be concentrated on examinations contributing most to genetic dose or somatic effects.

100 mm photofluorography is now in use for radiographic "spot films" during fluoroscopy, the extra capital cost being that of a 100 mm camera and the extra cost of a large (say 30 cm) intensifier instead of the more usual 23 cm intensifier. Improvements in image intensifiers may allow 100 mm photofluorography for routine radiography but the capital costs of replacing a "Bucky" with an image intensifier and 100 mm camera would be substantial. Financial savings accrue through the difference in costs between a 100 mm film and a large-size film after allowing for the loss of the income from recovering most of the silver content from processing solutions and scrap film. However, capital expenditure is incurred at year zero whereas savings accrue in the future and therefore need to be properly discounted, *e.g.*, as recommended by the Treasury (HMSO, 1980). An investment appraisal on the above lines would be unlikely to indicate a financial advantage for 100 mm photofluorography for applications other than spot films during fluoroscopy. However, if the whole of a radiodiagnostic department operated with 100 mm photofluorography only, there would be other savings *e.g.* cheaper processors, less chemicals, less storage space for films and less effort in filing them. In a large department these savings could be large.

Silverless imaging is a future possibility. For example a system could take the video signal from an image intensifier, digitize and store the data on a video disc. Video discs can, by means of a laser system, store 1000 to 10000 radiographic images. The cost of such a system would undoubtedly be substantial. Savings could also however be substantial in a large department. There would be no expenditure on films, chemicals and processors or large X-ray film stores and filing and retrieval of images could be significantly more efficient. Whether savings, after applying appropriate discounting, will be sufficient to meet the capital costs cannot be judged until commercial realization.

REFERENCE

Public Sector Economic Group, HM Treasury, 1980. *Investment Appraisal and Discounting Techniques and the use of the Test Discount Rate in the Public Sector*, (HMSO, London).

1981, *British Journal of Radiology*, *54*, 825–828

SEPTEMBER 1981

Proceedings of The British Institute of Radiology

Annual Congress Scientific Exhibition, April 9–10, 1981

Abstracts of papers presented at The British Institute of Radiology, Annual Congress Scientific Exhibition, April 9–10, 1981

Microfocal projection radiography: a new investigative technique, by J. C. Buckland-Wright and K. Twinn.
Scanning strategies—help or hindrance? by M. G. Adams, A. G. Gale, B. S. Worthington and K. Millar.
Preliminary results in the assessment of intracranial pathology by nuclear magnetic resonance imaging, by R. C. Hawkes, G. N. Holland, W. S. Moore and B. S. Worthington.
Objective assessment of mucosal detail in double contrast barium meals by spatial frequency analysis, by N. Russell, A. G. Gale, B. S. Worthington.
The accuracy of the plain film in assessing faecal contamination of the colon prior to barium enema, by B. Cramer and G. de Lacey.
Removal of radioactive contamination from skin, by M. V. Merrick, J. D. Simpson and Susan Liddel.
Serial quantitative bone scanning in breast cancer, by S. Parbhoo, H. Alani, B. Stoll, J. Agnew, Z. Varghese and K. Walmsley.
A method of non-invasive quantitative blood flow measurement, by P. J. Fish.
Vessel imaging and flow measurement with ultrasound, by H. B. Meire and P. J. Fish.
Pathological evaluation of CT scan images of lung, by R. Coddington, S. L. Mera, P. R. Goddard, N. Ring and J. W. B. Bradfield.
A new technique for radiation shielding in superficial X-ray therapy, by B. Baily, M. A. Coe and T. M. Hearnden.
Examples of micro focus radiography, by T. Atherton (Wells-Krautkramer Ltd.).
Dental applications of holography, by R. Dossetor, L. Wright, B. Keane and R. Juniper.
Teaching mediastinal anatomy: the CT correlation, by S. J. Golding.

MICROFOCAL PROJECTION RADIOGRAPHY: A NEW INVESTIGATIVE TECHNIQUE

By J. C. Buckland-Wright and K. Twinn

Guys Hospital, London SE1 9RT

The microfocal X-ray unit is a constant-potential X-ray generator with a 10–60 kV range and delivering a 1 mA current. The continuously evacuated X-ray column comprises two electromagnetic lenses which throw a greatly reduced electron image of the cathode onto the side of a solid, oil cooled, tungsten target. At 60 kV, 1 mA, the X-ray source size is approximately 6 μm in diameter, the smallest known to date. The object is brought close to the source to obtain high direct magnification up to $\times 15$ within a short camera. The use of rare earth screen/film combinations (Trimax α 16 and α 8) have reduced the exposure times. Noise inherent in these systems is overcome with magnifications of $\times 3$ or more. Phantoms containing grids show that the resolution increases with magnification providing a resolution of 25 μm at $\times$ 9.

Using post-mortem material, comparisons between the macroradiographs and the results from clinical X-ray units show that in the macroradiographs the image resolution, contrast range and magnification is far greater, providing a means for accurate mensural assessment of structures in bones and joints in normal and diseased conditions. The soft tissues are clearly outlined by air arthrograms and were even more clearly displayed by means of xeroradiography. In all cases stereopair radiographs are taken. Stereopsis provides augmented visual information.

In the examination of patients, the radiation dose is within clinically acceptable limits. Preliminary results were presented of time course studies of patients with rheumatoid and osteo-arthritis, renal osteodystrophy, fracture repair, scaphoid fracture and mammography.

SCANNING STRATEGIES—HELP OR HINDRANCE?

By M. G. Adams, A. G. Gale and B. S. Worthington

Department of Academic Radiology

and

K. Millar

Department of Behavioural Sciences,
University of Nottingham

The use in radiology of a set strategy for visually examining radiographs has often been advocated as an aid to improve detection of abnormalities through more efficient coverage of the film. Although intuitively plausible this advice is without any supportive experimental evidence. The following experiment was undertaken to examine this proposal in the detection of coin lesions.

Two groups of radiologically naïve subjects were first familiarised with the appearance of coin lesions and then shown a series of 30 chest films. Half of these films contained either one or two artificially produced coin lesions.

A microprocessor-based system was used both to present the films to the subjects and to generate the artificial lesions. The subjects were instructed to indicate whether the film was normal or contained lesions. The subjects' eye movements were recorded throughout the experiment.

All subjects were again tested a week later. Prior to this second session one group—the experimental group—was first trained to use a set strategy of scanning the radiographs. The control group had no such training, instead simply viewing chest films for a similar amount of time.

Whereas the performance of the control group increased slightly as a result of practice that of the experimental group declined. This finding is in accord with a cognitive model of perception which involves an interaction between the subject's schema and the stimulus information. Adherence to a strict scanning strategy led to the breakdown of this interaction and so produced poorer performance.

PRELIMINARY RESULTS IN THE ASSESSMENT OF INTRACRANIAL PATHOLOGY BY NUCLEAR MAGNETIC RESONANCE IMAGING

R. C. Hawkes, G. N. Holland and W. S. Moore

Department of Physics

and

B. S. Worthington

Department of Radiology and Human Morphology, University of Nottingham

The recently developed technique of NMR imaging which employs radio-frequency radiation is similar to X-ray computed tomography in providing a cross-sectional display of the body with excellent resolution of soft tissue detail. These images are essentially a map of the distribution density of protons in cellular water and lipids. NMR has the advantages of being non-invasive; avoiding the use of ionizing radiation; penetrating bone without attenuation and of being without known hazard.

In NMR imaging the scanning plane and slice thickness can be selected electronically and this has allowed high quality coronal and sagittal images to be obtained directly. This facility is valuable in defining the extent and topographical relationship of lesions in all three planes.

NMR images can also provide functional as well as structural information and there is evidence from current images that insight can be obtained into CSF dynamics and blood flow.

As with CT scanning, structures are identified and their shape, size and position defined. Alterations in tissue density are then sought and here there is a significant difference between the two methods. NMR imaging has a greater potential than CT for the selective examination of tissue characteristics, since, unlike the latter, where X-ray attenuation co-efficients alone determine image contrast, at least four separate variables contribute to the NMR signal.

NMR scans from several patients were shown, to compare the information available with that obtained from CT scans and conventional neuroradiological procedures.

OBJECTIVE ASSESSMENT OF MUCOSAL DETAIL IN DOUBLE CONTRAST BARIUM MEALS BY SPATIAL FREQUENCY ANALYSIS

By N. Russell, A. G. Gale and B. S. Worthington

Department of Academic Radiology, University of Nottingham

A study was carried out to compare the quality of the mucosal image achieved using four commercial barium sulphate preparations. Air-filled compartments lined by pig gastric mucosa were used as a model of the human stomach. The radiographic image obtained was evaluated on the basis of the spatial frequency model of vision; perception of fine mucosal detail is dependent on high contrast registration of the high spatial frequencies in the image.

The root mean square amplitude of the optical density is a function of the contrast and thus integration of different spatial frequencies with respect to amplitude will give a numerical value which will indicate how well the visual system can perceive detail in the radiograph.

The results show that EZ-HD provides a significantly better image than X-Opaque, Micropaque and Baritop. X-Opaque produces better results than Baritop or Micropaque, but the difference, although significant, is less great.

The morphology of barium sulphate particles in the four preparations was studied using the scanning electron microscope. EZ-HD and X-Opaque contain rough particles with a range of sizes. Baritop and Micropaque contain small smooth particles of more uniform size. This contrast is reflected in our results based on a measure of objective image quality. Anderson *et al.* (1980) have shown that with EZ-HD and X-Opaque a high proportion of large particles in the suspension settle out into grooves between the areae gastricae. This is one of the factors which contributes to the formation of a good mucosal image.

REFERENCE

Anderson, W., Harthill, J. E., James, W. B. and Montgomery, D., 1980. Barium sulphate preparations for use in double contrast examination of the upper gastrointestinal tract. *British Journal of Radiology*, *53*, 1150–1159.

THE ACCURACY OF THE PLAIN FILM IN ASSESSING FAECAL CONTAMINATION OF THE COLON PRIOR TO BARIUM ENEMA

By B. von Cramer

Radiology Department, Northwick Park Hospital

and

G. de Lacey

Clinical Research Centre, Harrow

Radiologists commonly use a plain abdominal radiograph prior to barium enema for assessment of likely faecal colon contamination. Surprisingly, many authors have used this plain film, and not the barium-filled films, to assess different colon preparation regimens.

A prospective survey of 448 patients assigned to four different preparation regimens was carried out. All were outpatients, and all studies were double contrast barium enemas. Three of the preparation regimens did not include colonic lavage. A plain film prior to each barium examination and the barium enema films were evaluated for faecal contamination. The results indicate that the plain film overstates the number of patients assessed as having a perfectly clean colon and underestimates the amount of faeces present. It is concluded that assessment of colonic preparation regimens should not be carried out on plain films alone. Moreover, it is suggested that a routine plain film in outpatients prior to barium enema should be discouraged: it is misleading, time consuming, expensive and represents unjustified radiation exposure.

REMOVAL OF RADIOACTIVE CONTAMINATION FROM SKIN

By M. V. Merrick, J. D. Simpson and Susan Liddel

Western General Hospital, Edinburgh

Despite proper precautions there is always some possibility of accidental skin contamination when radioactive substances are being handled. Other substances such as drugs and chemicals can also give rise to adverse reactions if they remain in contact with skin, but the presence of small quantities may be difficult to measure accurately.

Previous work has shown that flushing with plain water is relatively ineffective, and that pertechnetate is more adherent to skin than most other technetium-based radiopharmaceuticals. Even so the binding of pertechnetate is relatively weak compared with chromic chloride.

We have compared the efficiency with which pertechnetate and ^{51}Cr are removed by four different products, namely, soap and water, an aerosol foam detergent containing a chelating agent, a liquid detergent containing a chelating agent and a semi-abrasive skin cleanser.

The semi-abrasive cleanser was much the most effective at removing pertechnetate ($P < 0.01$). It was as good as the best of the other products in removing ^{51}Cr. Because its mode of action is non-specific it should be at least as effective at removing other forms of contamination. It should therefore probably be regarded as the agent of choice for general-purpose skin decontamination.

SERIAL QUANTITATIVE BONE SCANNING IN BREAST CANCER

By S. Parbhoo, H. Alani, B. Stoll, J. Agnew, Z. Varghese and K. Walmsley

Departments of Surgery, Radiotherapy, Medical Physics, Renal Transplantation and Radiology, Royal Free Hospital, London NW3

Scintigraphy is a sensitive technique for detecting skeletal metastases but small changes are difficult to interpret. In order to obtain earlier and accurate assessment of change we have used computerized quantitative scanning. Both the profile technique and a region of interest (ROI) technique to obtain a metastasis-to-normal-bone ratio have been used. These techniques and their advantages and disadvantages were displayed.

Bone scans using ^{99}Tc^{m} methylene disphonate have been carried out in 84 patients with advanced breast cancer. Serial studies at intervals of four weeks to six months have been carried out in 38 of these patients shown to have bone metastases.

The exhibit demonstrated the variation in the quantitation related to progressive disease, response to endocrine manipulation, ablative endocrine surgery, radiotherapy and cytotoxic chemotherapy. Recurrent disease as shown on the scans correlated with later clinical symptoms.

The use of a quantitative technique has allowed us to detect bone metastases or recurrence at an earlier stage and modify treatment accordingly.

A METHOD OF NON-INVASIVE QUANTITATIVE BLOOD FLOW MEASUREMENT

By P. J. Fish

Clinical Research Centre, Harrow, Middlesex HA1 3UJ

A consideration of some of the potential sources of error in transcutaneous flow measurement lead to the development of a multichannel pulsed Doppler instrument (MAVIS) having the following features:

1. Doppler frequency measurement in the presence of noise is made using a noise subtraction technique.
2. Doppler images of the vessel aid the operator in beam location and maintenance.
3. A method of angle measurement requiring two cross-sectional scans of the vessel-axis orientation measurement is used.
4. A correction is made for the effect of the low-frequency Doppler cut-off taking into account the velocity profile shape.
5. The effect of the finite length and width of the pulsed Doppler sampling volume on the measured velocity profile and flow rate are computed taking into account the velocity shape, variation of the sample volume width along the beam and vessel orientation.

The results of measurements made *in-vitro* and *in-vivo* have shown that the method is accurate and reproducible.

This work was supported by the Department of Health and Social Security and GEC Medical Equipment Limited.

VESSEL IMAGING AND FLOW MEASUREMENT WITH ULTRASOUND

By H. B. Meire and P. J. Fish

Clinical Research Centre, Harrow, Middlesex HA1 3UJ

By using a combination of pulsed ultrasound techniques and Doppler shift detection, an apparatus has been developed for imaging blood vessels within patients. Echoes returning from stationary structures are ignored and those returning from blood moving within the area of investigation give rise to the image which is closely analogous to the "moving target indicator" commonly used in military radar.

In order to obtain an image an ultrasound transducer is manually scanned over the area of interest and a vascular map is compiled over a period of several minutes. Three alternative views may be obtained, either a plan view, lateral view or cross-sectional view. Since the images represent only the areas of moving blood within vessels, abnormal narrowings of the vessels appear as defects in the image and occlusions result in failure to image a vessel. The examination is both painless and harmless and does not involve injection of contrast media or exposure of the patients to ionizing radiations. The technique is therefore valuable not only for the detection of vascular lesions but also for post-operative follow-up or for the assessment of response to medical treatment.

The apparatus is also direction-sensitive and arteries can therefore be reliably differentiated from the veins, and in the latest version of the equipment the arterial image is colour-coded red whilst veins are displayed in blue. The apparatus has also been developed to permit measurement of blood velocity, flow profile and vessel diameter. It is, therefore, now possible to measure accurately the volume of blood flowing within a vessel and early clinical trials of this facility are now underway in the Division of Radiology at the Clinical Research Centre.

The exhibit included examples of both normal and abnormal vascular images and examples of the functional data display and volume blood flow measurement.

PATHOLOGICAL EVALUATION OF CT SCAN IMAGES OF LUNG

By R. Coddington, S. L. Mera, P. R. Goddard, N. Ring and J. W. B. Bradfield

Bristol Royal Infirmary, Bristol

Computerized tomography (CT) is increasingly used in the study of respiratory disease. Correct interpretation of CT scan images requires correlation with known pathological lesions. In this study, lungs obtained at postmortem were inflation-fixed by formalin vapour in a specially designed cabinet. The fixed lungs were scanned producing images in the transverse plane at 13 mm intervals. After scanning, the lungs were sliced horizontally at 13 mm intervals to correspond with the CT scan images. The slices were X-rayed and Gough-Wentworth sections then prepared.

We found that the lungs could be maintained in an inflated condition, resembling the *in vivo* state, so providing a suitable preparation for CT scanning. Gough-Wentworth sections and radiographs of lung slices provided suitable material for correlative studies. Using these techniques the interpretation of lung images generated by the CT scanner can be validated by direct comparison with exact areas of lung tissue. Scans can be studied retrospectively to see whether particular lesions are visible, and quantitative studies of regional lung pathology are possible.

A NEW TECHNIQUE FOR RADIATION SHIELDING IN SUPERFICIAL X-RAY THERAPY

By B. Baily, M. A. Coe* and T. M. Hearnden

Departments of Physics and Radiotherapy, Westminster Hospital, London

Lesions within the first few millimetres of the skin are commonly treated using X rays generated in the superficial range, between 50 kVp and 150 kVp. The size and shape of such lesions are seldom identical with the applicators of the treatment unit and it is necessary to shield uninvolved tissue. This may be done using lead strips, lead sheet cut-outs, or, in the case of facial lesions, a lead sheet mask beaten onto a plaster cast of the face.

This latter process is difficult and time-consuming. To overcome these disadvantages a technique using low-melting-point alloys has been devised.

A low-melting-point alloy, of the type commonly used for high energy shielding, is sprayed onto a cast of the patient's face, building up to between 2 mm and 3 mm. Final thickness is dependent on X-ray energy and the need for adequate strength and coverage. It is not, however, critical since 2 mm affords adequate protection up to 250 kVp.

To provide absorption of secondary electrons a thin (0.3 mm) plastic shell is vacuum formed on the cast first and the alloy sprayed onto this. This has the additional advantages of allowing the mask to be lifted without damage and providing a comfortable, hygienic surface in contact with the patient. The treatment "window" and nasal airways are cut with a hot soldering iron and dental burr.

EXAMPLES OF MICRO FOCUS RADIOGRAPHY

By T. Atherton

Wells Krautkramer Ltd., Sutton Coldfield, West Midlands

The main advantage of micro focus radiography is the possibility of projecting small samples onto a large X-ray film but maintaining good resolution and quality. Dr. J. C. Buckland-Wright of Guy's Hospital Medical School has used this to demonstrate the effect different drugs have on arthritic joints of small animals.

He shows how it is possible to produce measurements to assess the results. The X-ray equipment used has a focal spot size of less than 10 μ operating to 30 kV at 1 mA beam current. Magnifications up to × 20 are possible. X-ray examination of the detailed structure of organs and biological specimens is possible providing the specimens to be radiographed are only several millimetres thick. The E12 equipment, now marketed by Wells-Krautkramer Limited and developed by Harwell N D T Central Laboratories, operates at 80 kV and up to 1 ml with a 10 μ focal spot, and can also be used for this kind of research and investigation. The extra kV offer more flexibility; the equipment can be used with larger animals and does not exclude live animals.

DENTAL APPLICATIONS OF HOLOGRAPHY

By R. Dossetor, L. Wright, B. Keane and R. Juniper

Royal Sussex County Hospital, Brighton

In oral surgery, dental models are required to assess changes both before and after surgery. Storage of these models is difficult and is often impractical on any large scale. Holography represents a potential new method of storing these models as three dimensional images. Further, with bleached transparent holograms there is potential scope for direct measurements to be made on and in the three dimensional images. Anatomical comparisons are facilitated by superimposing two images taken before and after the event, whereupon both the direction and magnitude of changes become immediately apparent. The equipment required to produce the holograms is relatively simple, consisting of a single beam "Denisyuk" assembly powered by a He-Ne laser of up to 10 mW. Agfa-Gevaert Holotest film type 8E75 is used, with appropriate development and bleach to provide white light holograms which may be viewed by a suitable compact source of light.

TEACHING MEDIASTINAL ANATOMY: THE CT CORRELATION

By S. J. Golding

CT Scanning Unit, Royal Marsden Hospital, Sutton, Surrey

The mediastinal pattern seen on conventional chest radiography is a complex summation shadow made up of the images of the thoracic viscera and the surrounding lung. The pulmonary lobes extend into the mediastinum between the viscera so that a significant amount of lung is contained within the mediastinal silhouette.

The mediastinal pleural reflections form the boundaries of the lung and may be visible where tangential to the X-ray beam, by virtue of the difference in density between the lung and the underlying structures. In addition, there are areas where the right and left lungs are adjacent and separated by pleura alone. These boundaries form the mediastinal "lines".

Appreciation of the areas of lung in the mediastinum is valuable in practice since pulmonary pathology may be obscured by the mediastinal density. Similarly an understanding of the mediastinal lines is essential to the diagnosis and assessment of mediastinal disease. Mediastinal anatomy is, therefore, an important teaching topic.

Computed tomography (CT) provides an appropriate method of displaying the mediastinal anatomy for two reasons; first, it is cross-sectional and therefore free of superimposition effects, and second, CT and conventional radiography have the same physical basis; display is derived from X-ray attenuation. The way in which juxtaposition of soft tissue and lung contribute to the conventional radiographic appearance is therefore readily appreciated from CT sections.

In this exhibit a teaching model consisting of correlated conventional radiographs, tomograms and CT scans has been constructed to show how CT may be used to explain the conventional radiographic anatomy of the mediastinum.

---

*Present address—Radiotherapy Department, St. Luke's Hospital, Guildford, Surrey.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).

Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 36 Portland Place, London W1N 3DG.

Fellowships and Grants for Cancer Research

The International Union against Cancer invites applications for: Cancer Research Campaign fellowships (deadline October 1); Eleanor Roosevelt International Cancer fellowships (deadline October 1); Yamagiwa-Yoshida Memorial International Cancer Study grants (deadline December 31); and International Cancer Research Technology Transfer Programme grants (applications as soon as possible). Details and application forms from: UICC, rue du Conseil-Général 3, 1205 Geneva, Switzerland.

The International Agency for Research on Cancer (WHO) also invites applications for training fellowships, 1982–3. Deadline January 31, 1982. Details: Research Training & Liaison Programme, IARC, 150 cours Albert-Thomas, 69372 Lyon, Cedex, 02, France.

Contrast Media. Fundamentals and Clinical Application

The Department of Diagnostic Radiology of the University of Rochester will offer a two-and-a-half day course on Contrast media: fundamentals and clinical application, September 21–23, 1981. The philosophy of this course is to review the fundamental chemical, physical, physiological, and toxicological properties of radiopaque media and to describe the relationship and importance of these properties to radiological application and diagnoses. The curriculum will provide a thorough introduction to contrast media for residents, Fellows, and junior faculty as well as a refresher course for the more experienced radiologist. The knowledge conveyed should be useful in the clinical setting and in the laboratory. For further information, contact Harry W. Fischer, M.D., Chairman, or Michael R. Violante, Ph.D., Course Director, Department of Radiology, PO Box 648, University of Rochester Medical Center, Rochester, New York 14642; phone (716) 275-2617.

European Association of Radiology
II European Symposium on Intervention Radiology

Venice, Italy, September 28–October 3, 1981. Information: Istituto di Radiologia Università, Viale Benedetto XV, 10, 16132 Genova, Italy.

The Faculty of Radiologists of The Royal College of Surgeons in Ireland

21st Anniversary Meeting, Dublin, October 2–3, 1981: jointly with The British Institute of Radiologists, The Royal College of Radiologists, and The Royal Society of Medicine. Diagnostic and therapy sessions; topics to include radiology in renal failure and radiology of trauma. The BIR Presidential Address for 1981, "Chest radiology—guesswork or science?" will be given by Dr. D. H. Trapnell. Technical exhibition. Details: Miss A. Daly, Faculty of Radiologists, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2.

Symposium of Radiological Physicists
Bratislava, Czechoslovakia, October 5–7, 1981

Topics proposed are: radiation dosimetry of high-energy electrons, X and γ rays, and neutrons; computer planning of radiotherapy treatment; radiation protection of patients and staff during radiotherapy. Languages: Slovak, Czech and English. Registration fee $50. Further details from the Slovak Medical Society, Congress Office, Mickiewiczova 18, 883 22 Bratislava, Czechoslovakia.

Diagnostic Imaging in Medicine Course

October 11–23, 1981, Estoril, Portugal. Sponsored by NATO Advanced Study Institute and The George Washington University Medical Center. Registration $95.00 (no other charge). CME Category I credits available. Subjects include: nuclear, ultrasound, CT, NMR, and X-ray imaging, clinical and experimental. For application to attend write: Richard C. Reba, M.D., Division of Nuclear Medicine, George Washington University Hospital, 901 Twenty-Third Street, NW, Washington, DC, 20037. Phone: (202) 676-3458.

Royal College of Physicians and Surgeons of Glasgow Symposium on "Choices in Organ Imaging—When to do What"

This symposium will be held in Glasgow on Wednesday, October 14, 1981. Chairmen: Dr. J. K. Davidson, Dr. W. B. James and Dr. J. G. Duncan. Speakers: Dr. S. R. Wild, Dr. E. Barnett, Dr. D. A. R. Robertson, Dr. J. C. Rodger, Prof. I. Isherwood, Prof. J. J. K. Best, Dr. M. V. Merrick and Dr. P. Morley. Registration fee £10. Applications and information: The Hon. Secretary, Royal College of Physicians and Surgeons of Glasgow, 234–242 St. Vincent Street, Glasgow G2 5RJ (phone 041-221 0241).

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Radiobiology Work-in-Progress Meetings

Meetings during the coming year at the Institute include "Subcellular targets, including ultrastructural damage", November 20, 1981; a general meeting on February 26, 1982 and "Late damage to normal tissues after radiotherapeutic doses" on May 21, 1982. The all-day Saturday meeting will be on November 21, 1981, on "The effects of small doses—the basis of radiation protection". Proffered papers for the November meeting should reach Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, by September 20.

Please note all meetings will be held at the BIR's new address, 36 Portland Place, London W1.

The Radiological Diagnosis and Treatment of Thyroid Disease
Wednesday, November 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held at the Institute, 36 Portland Place, London W1. The meeting will cover all aspects of thyroid disease, including the use of isotopes. Enquiries to: Dr. John Frank, The Wessex Regional Department of Nuclear Medicine, Southampton General Hospital, Southampton SO9 4XY.

Safety Review and Inspection of Nuclear Power Plants

The International Atomic Energy Agency will hold a seminar in Vienna from November 23–27, 1981. Further information and participation forms from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4OJ (phone 01-211 6850). Applications by September 30.

Forthcoming events and notices

Paediatric Radiology 1981

Great Ormond Street, London, November 26–27

This annual two-day course is designed for consultants and senior registrars. The theme will be the gut; other topics covered will include jaundice, hypertension and the neonatal big head. Speakers will include paediatricians, paediatric surgeons and endoscopists; there will be opportunity for open discussion.

There are a limited number of places. Cost £40. Full details: Dr. I. Gordon, Department of Paediatric Radiology, Hospital for Sick Children, Great Ormond Street, London WC1 (telephone 01–405 9200).

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1. Enquiries to 36 Portland Place, London W1N 3DG.

Fourth Radiological and Radio-Anatomical Course

Val d'Isère (French Alps), January 17–23, 1982. Professors G. Salamon, V. Bismuth and J. L. Lamarque. Will be devoted this year, as in the preceding years, to the correlations between normal anatomy and radiological investigations as well as the correlation between anatomical pathology and radiological, CT or ultrasound images.

The themes of the course will be orbital pathology (in collaboration with Dr. Jacqueline Vignaud) sella tumours, biliary pancreatic problems, the unprepared abdomen, thoracic pathology, hysterosalpingography and digital angiography.

For information and registration write: Mme. Jacqueline Peloux, Laboratoire de Neuroradiologie et Radiologie Vasculaire, Hôpital de la Timone, 13385 Marseille Cedex 5, France (tel (91) 49.40.41). Registration fee: 800F (700F to members of CEPUT, 250F to students).

Quantities and Units for use in Radiation Protection

Scientific meeting and exhibition, National Physical Laboratory, Teddington, Middlesex, Tuesday, January 26, 1982. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

The Mayneord Symposium

Friday, February 19, 1982. This meeting is being organized by, the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. It will be an all-day meeting to be held at the Royal Society, in Carlton House Terrace, London. The theme for the meeting will be "The future in radiology" as seen by distinguished workers in a number of branches of radiological science.

The Natural Radiation Environment

Tuesday, March 30, 1982, at the Central Electricity Generating Board, Sudbury House, 15 Newgate Street, London EC1. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Society for Radiological Protection

Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ. Abstracts to be received by July 15, 1981.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on The contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A. M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

5th South African

International Radiological Congress

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas sponsors, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

Correspondence—*continued.*
X-ray tube lifetime and image quality in computed tomography.
C. B. Smith; P. C. Shrimpton and D. W. Dewhirst
Hybrid real time/B scan ultrasonic system.
R. E. Richardson and P. Davies; S. R. Wild and W. N. McDicken

Proceedings of The British Institute of Radiology. 822
Radiographic systems: what is best? March 18, 1981.
Annual Congress Scientific Exhibition, April 9–10, 1981.

Forthcoming events and notices. 829

Book reviews

Abdominal ultrasound in the cancer patient 757

Fundamental and clinical bone physiology 767

Radiotherapy treatment planning (Medical Physics Handbooks 7) 781

Management of persons accidentally contaminated with radionuclides (NCRP Report 65) 798

Uroradiology 821

INSTITUTE OF UROLOGY
(University of London)
in association with St. Peter's Hospitals

URO-RADIOLOGY WEEKEND

4th and 5th December 1981

To be held in the Lecture Theatre, Institute of Urology, 172 Shaftesbury Avenue, London WC2H 8JE.
Films for the quiz will be displayed Friday lunchtime.

Friday 4th December 1981. 2.00–6.00 p.m.

Developmental abnormalities of the upper urinary tract.	Dr. Donald Shaw, University College Hospital, London.
Prune Belly Syndrome	Dr. M. J. Kellett, St. Peter's Hospitals, London.
Renal Cystic Disease in Children	Dr. Christine Hall, Hospital for Sick Children, Great Ormond Street, London.
Urethrography	Dr. Caroline Parks and Dr. K. Patel, St. Peter's Hospital, London.
Radiology Quiz	

Saturday 5th December 1981. 9.30 a.m.–4.00 p.m.

Evaluation of the hypersensitive patient	Dr. Judy Webb, St. Bartholomew's Hospital, London.
Long term follow-up of patients after renal angioplasty	Dr. Eric Martin, New York.
Therapeutic applications of percutaneous nephrostomy	Professor Rolf Günter, Mainz.
Needling Nodes	Dr. N. B. Bowley, Hammersmith Hospital, London.
Calyceal Deformities	Dr. H. M. Saxton, Guy's Hospital, London.
Renal Failure Radiology 1981	Professor T. Sherwood, Cambridge.

Fee: £40

Applications to Courses Secretary, Institute of Urology, 172 Shaftesbury Avenue, London WC2H 8JE. Tel: 01–836 5361, ext. 30, from whom detailed programmes may be obtained.

VOL 54 NO 645 **SEPTEMBER 1981**

The British Journal of Radiology

Contents

Page

A reappraisal of the genetic consequences of diagnostic radiology in Great Britain. 719
B. F. Wall, S. Rae, S. C. Darby and G. M. Kendall

Coronary collateral response and myocardial function. 731
J. K. Walker, P. R. M. Jones and R. H. Harding

The three types of criss-cross heart: a simple rotational anomaly. 736
S. M. Tadavarthy, A. Formanek, W. Castaneda-Zuniga, J. H. Moller, J. E. Edwards and K. Amplatz

Computerized tomography versus angiography in the staging of malignant renal neoplasm. 744
P. Probst, H. M. Hoogewoud, M. Haertel, E. Zingg and W. A. Fuchs

Inversion of the right hemidiaphragm shown on ultrasound examination. 754
S. H. Lowe, D. O. Cosgrove and A. E. A. Joseph

Atlanto-occipital and atlanto-axial dislocations with spinal cord compression in Down's syndrome: a case report and review of the literature. 758
G. D. Hungerford, V. Akkaraju, S. E. Rawe and G. F. Young

Isotope bone imaging in suspected scaphoid trauma. 762
E. B. Rolfe, N. W. Garvie, M. A. Khan and D. M. Ackery

A study of the effect of sodium/meglumine ioxaglate (Hexabrix) on thyroid function. 768
R. G. Grainger and G. W. Pennington

New modalities in cancer treatment: heavy charged particles. 773
E. J. Hall

Tolerance of brain to multiple courses of radiation therapy. I. Clinical experiences. 782
A. Dritschilo, J. E. Bruckman, J. R. Cassady and J. A. Belli

Tolerance of the mature human central nervous system to photon irradiation. 787
D. R. Wigg, K. Koschel and G. S. Hodgson

Repair during fractionated irradiation of the mouse bladder. 799
F. A. Stewart, V. S. Randhawa, B. D. Michael and J. Denekamp

Technical notes. 805
  A new technique for radiation shielding in superficial X-ray therapy.
    B. Baily, M. A. Coe and T. M. Hearnden
  A transportable gamma camera service: initial technical results.
    M. A. Smith, M. V. Merrick, V. F. Storjohann and A. J. Wong

Case reports. 813
  Retroperitoneal angiomatous lymphoid hamartoma demonstrated by ultrasound.
    S. Hamilton and D. McInerney
  Ultrasound diagnosis of hydrops fetalis due to fetal tachycardia.
    I. M. Shirley, B. A. Richards and R. H. T. Ward
  Triple gall bladder.
    D. R. Foster

Correspondence. 819
  Léri's pleonosteosis.
    D. G. Shaw
  Ultrasound in hepatoma.
    J. F. Calder
  Mullard 4 MV linear accelerator at Newcastle upon Tyne.
    W. M. Ross and M. J. Day

(continued on inside back cover)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
36 Portland Place, London W1N 3DG

ISSN 0007–1285
17030

149.82

October 198

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis

Radiation oncology

Nuclear medicine

Ultrasound

Radiological physics

Radiobiology

Radiation protection

and related [illegible]

Published b
The British Institute of Radiolog

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

J. L. HAYBITTLE, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
C. H. JONES, BSC., PH.D., F.INST.P.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., CH.B., F.R.C.R., F.R.A.C.R. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14). (From January 1, 1982: £65·00 ($145), single copies £7·00 ($16); postage extra on all orders received after April 30, 1982.)

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
36 PORTLAND PLACE, LONDON W1N 3DG
Telephone: 01–580 4085 and 580 4189. Cable Address: "Britology, London W.1."

President: M. J. DAY, B.A., PH.D.

Hon. Secretaries:
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
JANET HUSBAND, M.R.C.P., F.R.C.R.

Hon. Treasurer: D. PACE

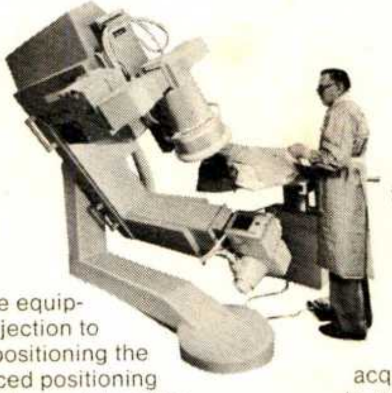
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company offers superior multi-axis vascular imaging equipment today ...and tomorrow?

General Electric Company of U.S.A:*
Making new technology accessible.



The unique isocentric design of today's L/U-Angio multi-axis vascular system keeps anatomy centered as the equipment is moved from projection to projection... without repositioning the patient. And, this advanced positioning system's Fluoricon L300 image intensifier is fully compatible with digital fluoroscopy technology, to permit optimum clinical performance far into the future.

Such upgrade capability is also designed into other General Electric of U.S.A. imaging systems: In computed tomography, the Continuum concept means that new capabilities can easily be added to every existing CT/T system. And in nuclear diagnostics, by adding a data acquisition and analysis system to an existing MaxiCamera 400T system, complete Emission Computed Tomography can be performed.

Upgrade capability. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

Frankfurt/M., Tel.: 06 11/7 60 73 69 • Wien, Tel.: 24 14 51 • Brüssel, Tel.: 660 2010 • Kopenhagen, Tel.: 2 86 86 00 • Mailand, Tel.: 753 1351 • Breda, Tel.: 76 22 54 15 • Lissabon, Tel.: 36 71 55 • Madrid, Tel.: 252 5100 • Göteborg, Tel.: 42 09 70 • Zurich, Tel.: 47 50 30

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

Diagnostic Radiologist

Diagnostic Radiologist wanted, with fellowship or eligible, to join radiological group in Edmonton, Alberta, Canada. Hospital and office practice. Applicant should have training in special procedures and/or ultrasound.

Please reply to:
Dr. W. J. Taylor, M.B., Ch.B., D.M.R., F.R.C.P.(C.)
#360 10830-Jasper Avenue
Edmonton, Alberta
Canada T5J 2B3

BEIRUT

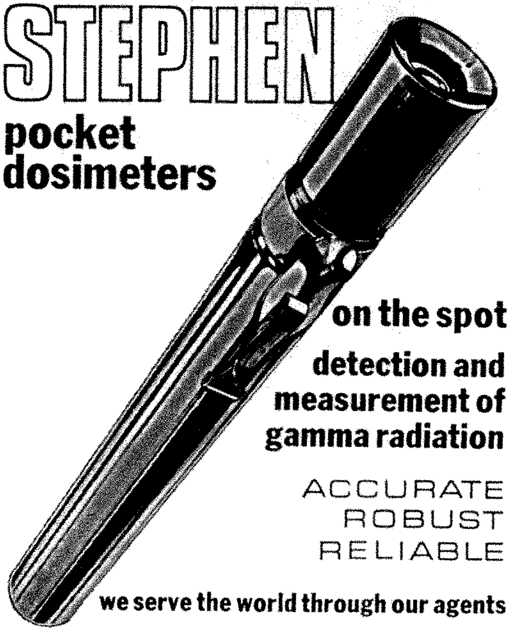
Required—Brain CT Scan Radiologist for private hospital.

Very attractive salary.

Address:
Dr. TOHME ALMABANY
55 Piccadilly, W1

STEPHEN

pocket dosimeters



on the spot detection and measurement of gamma radiation

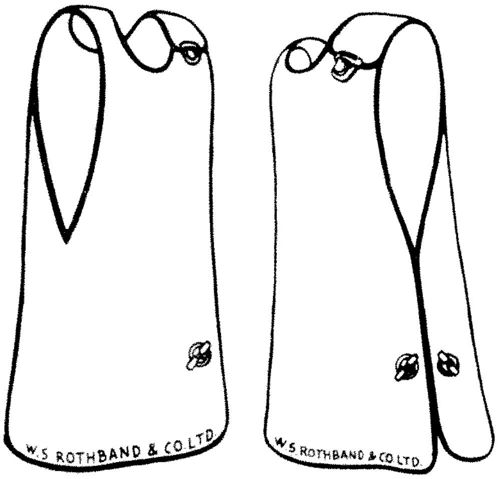
ACCURATE
ROBUST
RELIABLE

we serve the world through our agents

R·A·Stephen
AND COMPANY LIMITED
Miles Road Mitcham CR4 3YP Tel 01-648 1668/9

DOCTOR "C" TYPE DOUBLE-SIDED APRON

Right side closed, left side has push-in-clip shoulder fastening, (or if "Velcro" preferred, please state on order).



Super-flexible–Multi-layered.

Foam padded shoulders.

Standard size is 24 in (61 cm) wide. Ladies slim fitting 21 in (53 cm) also available.

Lengths, choice of 33 in (84 cm), 36 in (91 cm), 39 in (99 cm), 42 in (107 cm).

Washable PVC colours, choice of royal blue, white, green, yellow, red.

Lead equivalents, choice of 0.25 mm, 0.35 mm, 0.50 mm.

This Apron has been specially designed by our Company for operators who stand "right-side-on" and who require protection without a gap on the right hand side.

W. S. ROTHBAND & CO. LTD
Telephone 061–834 1303

21 Elizabeth Street
Manchester M8 8WT, England

Established 1860

New: for the treatmen of malignant effusions

Coparvax is a freeze-dried preparation of Corynebacterium parvum. When injected into previously-aspirated pleural or peritoneal effusions, Coparvax has been shown to be extremely effective at preventing recurrence and easing the associated symptoms.

In addition, Coparvax has a remarkably low incidence of side-effects, unlike many other treatments, some of which may require concomitant narcotic analgesia.

For further information on this advance in the management of malignant effusions please contact our Scientific Services Division at the address below.

PRESCRIBING INFORMATION

Presentation Vial containing 7mg (dry weight of the inactivated *Corynebacterium parvum* organism WFL strain CN 6134) with thiomersal, in a freeze-dried form. **Uses** Alleviation of malignant pleural effusions and malignant ascites. **Dosage** 7-14mg recommended, although some patients have responded to lower doses. **Administration** Freeze dried Coparvax should be reconstituted with 1ml of physiological saline for injection and diluted in a further volume of 10-20ml prior to injection. The suspension should be injected, within 24 hours of reconstitution, into the pleural or peritoneal cavit via the paracentesis needle immediately after th effusion has been aspirated. Injection may be repeated, if necessary, at intervals of one to four weeks. **Contra-indications** During pregnancy, an patients with known hypersensitivity to thiomersa **Precautions** The incidence and severity of side-effects attributable to Coparvax administered intrapleurally, appears to be intensified if given within 10 days of thoracotomy and lung resection probably due to enhanced systemic absorption c Coparvax. Coparvax should not be given during the immediate post-operative period. Following intrapleural or intra-abdominal administration, leakage of Coparvax into subcutaneous tissues may result in local tenderness. Intense fibrinous reaction in the pleural and peritoneal cavities ha been observed following local administration of Coparvax. Intestinal obstruction due to the formation of adhesions is a theoretical possibility, although it has not been reported as a complication of Coparvax administration. **Adverse effects** Fever occurs in 10 to 40% of patients following intracavitary injection. Abdominal pain or mild abdominal discomfort has been reported in som 20% of patients following intraperitoneal instillatic Nausea and vomiting may occur in a minority of patients following intracavitary administration o Coparvax. **Basic NHS Cost** Single vial (7mg), £30 (PL3/0097).

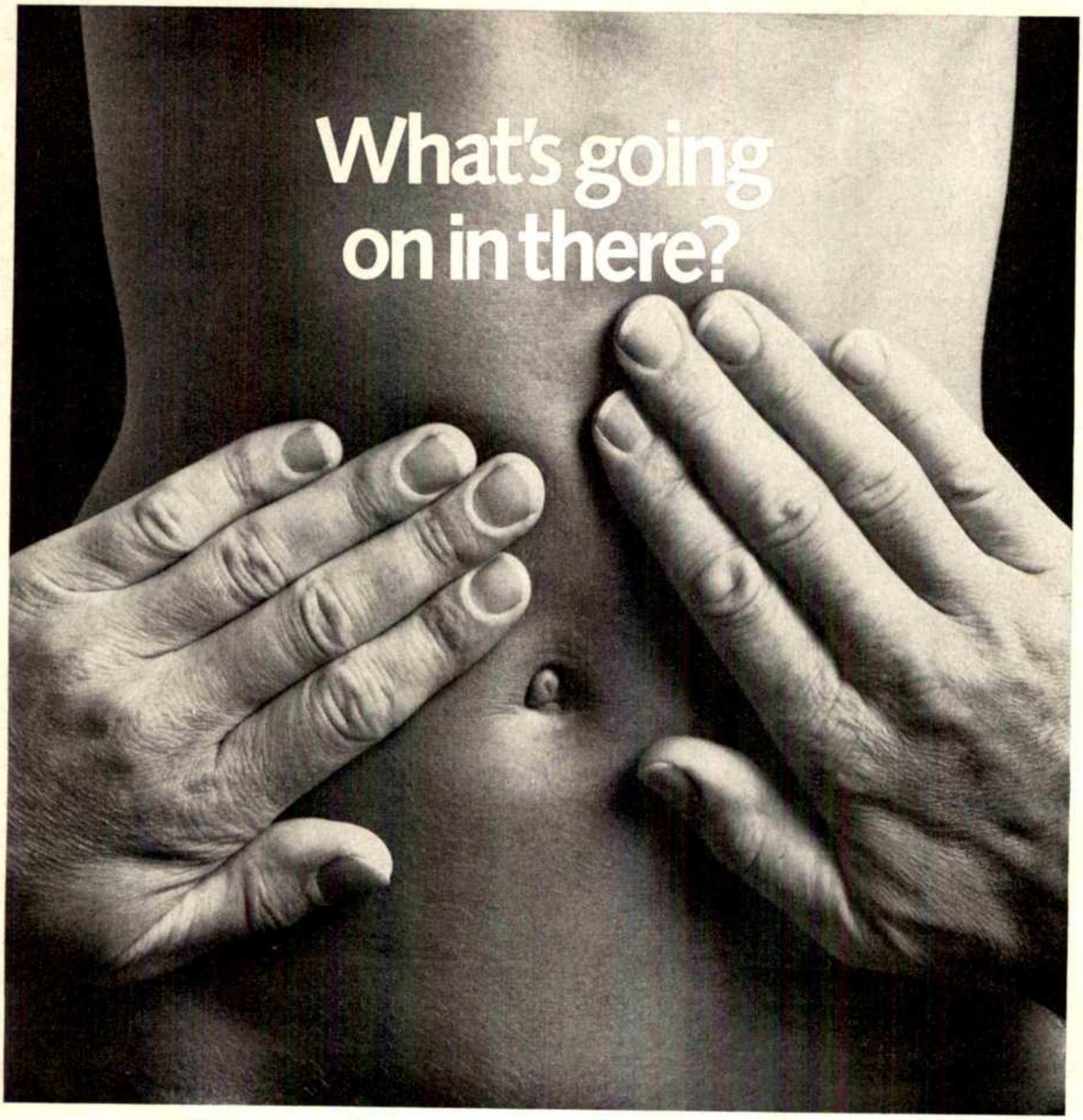
Coparvax*

Corynebacterium parvum

when the quality of life is the primary concern

Calmic Medical Division
The Wellcome Foundation Ltd.
Crewe, Cheshire
(Tel: 0270 583151)

*Trade Mark



What's going on in there?

Trust baritop to tell you

Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

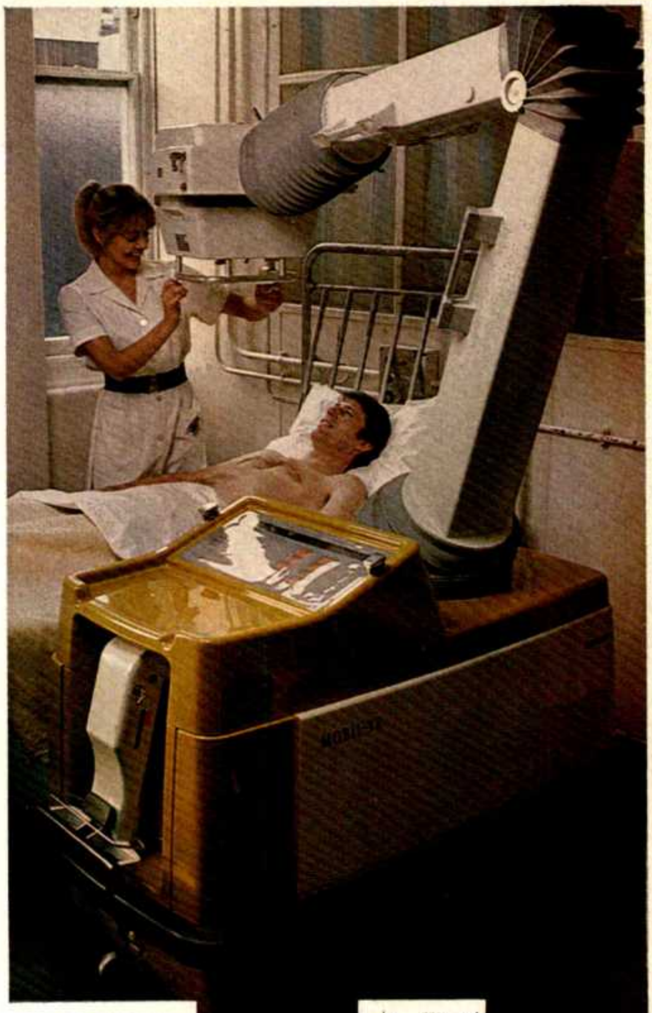
Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.

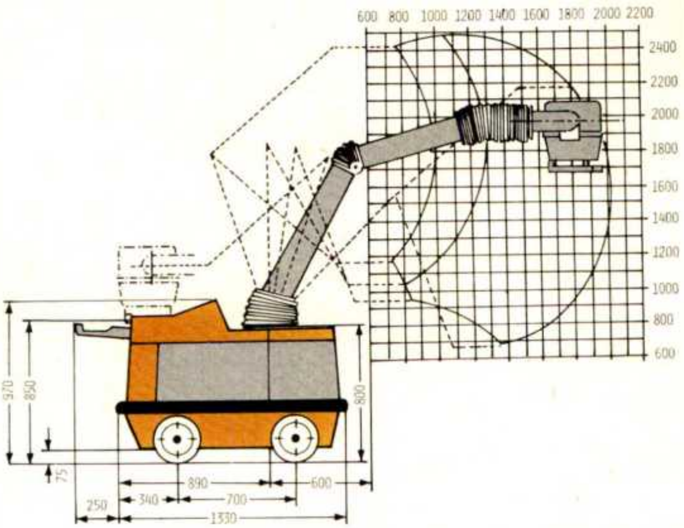
SIEMENS

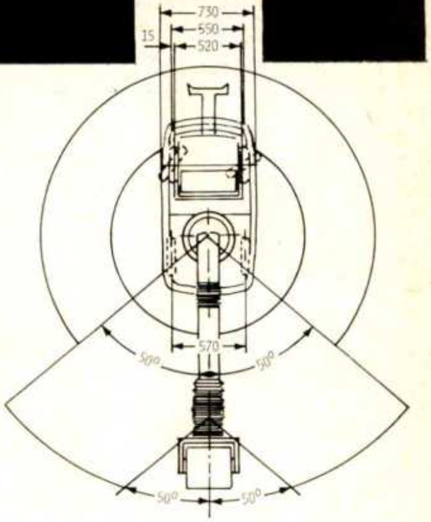
Mobil XR – brings a microprocessor controlled, aseptic mobile radiography unit to the patient.



The battery-powered MOBIL XR is self-propelled and self-contained with microprocessor controls providing full power exposures at 20 kW time after time. The adjustable counter-balance arm and a wide range of alphanumerically displayed exposure parameters allow sharp image examination of any organ or limb. Aseptic design with touch controls and total enclosure fo all components make it ideal for theatre use. Infinitely variable speed control makes it easy to manoeuvre and pull-out cable allows simple recharging at any power point.

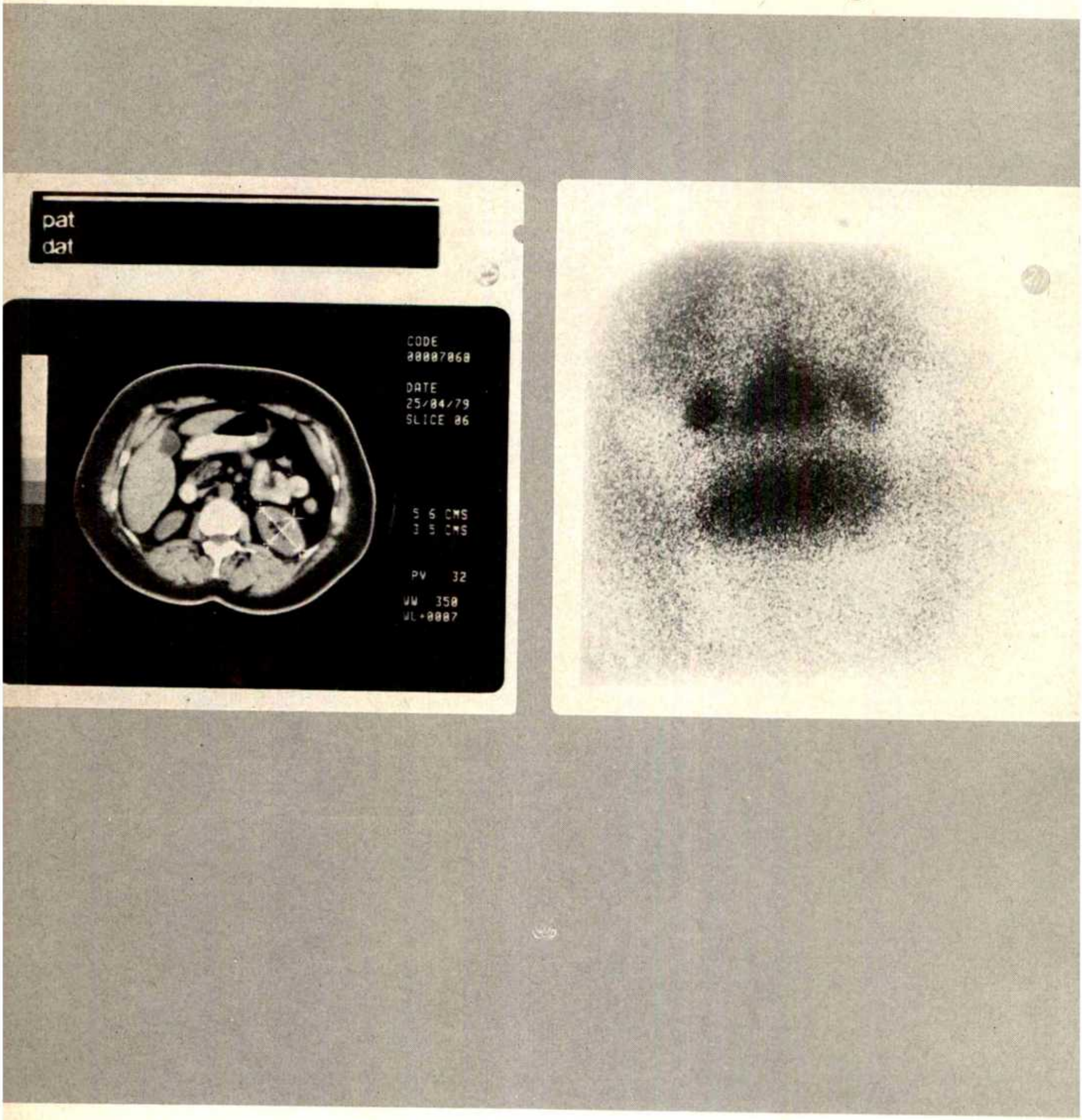
For further details or a demonstration contact:
Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS.
Tel. Sunbury (09327) 85691.





In the world of mobile radiography Siemens has the answer.

The Oldelft 100mm system is



10x10 cm sheetfilm photography: the most economic

One of the assets of the Oldelft 100mm sheetfilm system is the CRT image display recording line. It comprises the Catodica camera-back and offers distinct advantages over instant camera systems in CT scanning, ultrasound, nuclear medicine and thermography:
the exposures are made on transparent film, have a much better contrast and definition, and represent the full grey scale; the use of 100mm sheetfilm gives a considerable saving of film costs:
the supply of fifty 100mm sheetfilms (= one 'Delpack' daylight loading film pack) and the take-up capacity of 25 exposures make sure that an entire examination can be recorded without interruption;

ldelft products are sold by the leading
ray equipment manufacturers

more efficient and more economic

solution for CRT transparencies

genuine hands-off-the-camera system, thanks to the motor-driven film transport.
For all these reasons, the Oldelft way of CRT image recording on 100mm sheetfilm is to be preferred.
The Oldelft 100mm system is a sure way in every respect to improve the quality of your images and to save time, money and space.

Oldelft: quality and reliability

Oldelft
nv Optische Industrie De Oude Delft

Holland, Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011

U.S.A., Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, telex 08

Germany, Postbox 5420, D 6300
Giessen/Lahn, Tel. (0641) 4 10 49, telex 482930

Japan, Osaka, Postbox 1042.
Tel. (06) 309 09 61, telex 523 4170

SIEMENS
When programmed x-ray diagnosis is preferred, we have the ideal combination
SIREGRAPH-C
SIEMENS
Programme
Manual

The multipurpose Siregraph C automatic x-ray table has enhanced routine diagnostic capability, including aniography of the body trunk and lower extremities.

The escutcheon of the Tridoros 712 MP generator puts all the radiographic parameters at your fingertips by means of microprocessor technology.

Programmed radiographic factors may be inserted by the Superintendent Radiographer or Radiologist and these factors are retained permanently under lock and key. This 70kW 12 pulse machine maintains high voltage accuracy yet offers extreme flexibility with provision for 49 programmes each for radiography and planigraphy.

For full details contact: Siemens Medical Group,
Siemens Limited, Windmill Road, Sunbury-on-Thames,
Middlesex TW16 7HS. Telephone: (09327) 85691.

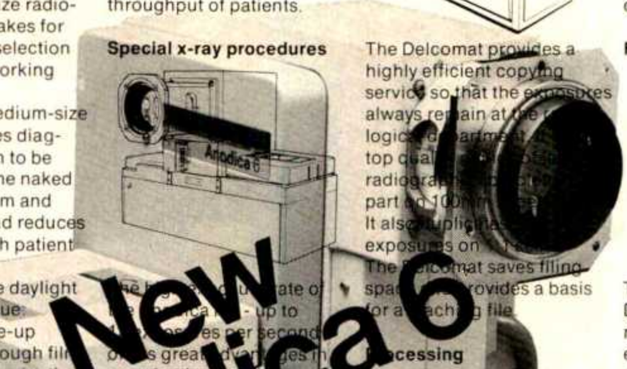
Siemens–the ultimate in cost effective x-ray diagnosis

Oldelft offers you more than just a good camera... it gives you a complete system.

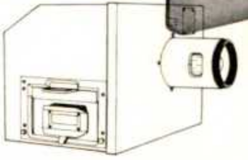
Oldelft makes high quality 100mm cameras for image intensifier photography and CRT display recording.
But that's not all. Oldelft also makes a whole range of products that simplify the entire film handling operation after exposure. Together, these products make up the Oldelft 100mm daylight system. It's based on the use of 10x10cm sheetfilm. But mainly it uses apparatus already available in radiological departments. Which means it fits smoothly into the department's work routine.
Nothing has to be changed.

Advantages of the 100mm sheetfilm system

- the 100mm system works with sheetfilm - as you are used to in large-size radiography - which makes for easy sorting and selection and an efficient working routine.
- it works with medium-size film, which enables diagnostic information to be interpreted with the naked eye. It also cuts film and chemical costs and reduces x-ray dose for both patient and doctor.
- it works with the daylight magazine technique: its supply and take-up magazine hold enough film for a complete examination. No interruptions. No fussing with cassettes. Result: less time needed [illegible] examinations, be[illegible] throughput of pa[illegible]
- t[illegible] 100mm sys[illegible]m is flex[illegible] [illegible]mponents can be cho[illegible] [illegible] hospital's ind[illegible]



General x-ray diagnosis

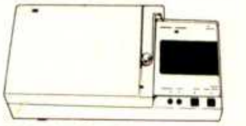


The Anodica-2 image intensifier camera is capable of up to two exposures per second. It is especially suitable for use in cases of gastro-enterology, neurology, urology, orthopaedics, gynaecology and paediatrics. Anodica techniques offset the disadvantages experienced with conventional large format radiography. Handling operations are considerably reduced and there is a marked increase in throughput of patients.

Special x-ray procedures

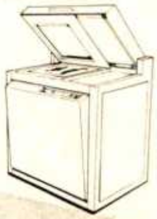
[illegible] ate of [illegible] - up to [illegible] es per second [illegible]s great [illegible] ges in examinati[illegible] general [illegible] s[illegible] angiography[illegible] angiography. Motion blur is [illegible]ed, focal spot of the x-ray tube is smaller and x-ray dose is low.
Use of Anodica exposure technique means that catheterization and image intensification can be simultaneous. It is therefore not necessary to move the patient.

CRT display photography



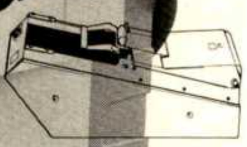
With the Catodica camera-back for CRT display recording of ultrasound, gamma cameras and CT scanners, a substantially better quality image is obtained than is possible on positive paper film from instant camera-backs. The Catodica works with a magazine that can be loaded in full daylight.
The automatic film transport means great facility and quick examination.

Film copying



The Delcomat provides a highly efficient copying service so that the exposures always remain at the [illegible] logic[illegible] [illegible]artment[illegible] top qual[illegible] radiogra[illegible] part [illegible] 100m[illegible] It als[illegible]plica[illegible] exposures on [illegible] The [illegible]comat saves filing spa[illegible] [illegible]rovides a basis for a [illegible]ch[illegible]g file.

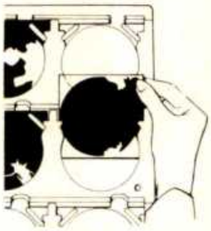
[illegible]cessing



By means of the Film Feeder, 100mm sheetfilms can be processed automatically and in daylight, using normal large-size film processors without modification.
Small daylight processors for instant use with the camera are also available.

Viewing

For quick quality check and easy diagnosis, exposures can be mounted in correct order in the Cadrix, a simple plastic holder, which is placed on the viewing box.
For large group discussion, as for example during teaching sessions, pictures can be enlarged through the Heliomat viewer or by means of an overhead projector.



Framing

The manually operated Delcadro offers a simple method of mounting six exposures together in an economical paper frame.
In this way pictures selected after viewing in the Cadrix can be kept together for orderly presentation and are readily filed. An automatic version of the Delcadro is also available. It is especially effective for handling large quantities of film.

In brief

The 100mm system offers an efficient method of picture registration for a large number of hospital examination areas.
It reduces cost, saves time.
For simple film handling, a sophisticated package of accessories is available.
And remember - 100mm film offers a basis for planning substantial reduction in filing space.

Please send me more information about the 100mm system.
I am particularly interested in:

☐ how to cut film costs	☐ 100mm spot film photography
☐ standardization on 10x10 film	☐ 100mm CRT photography
☐ filing space reduction	☐ 100mm copying services

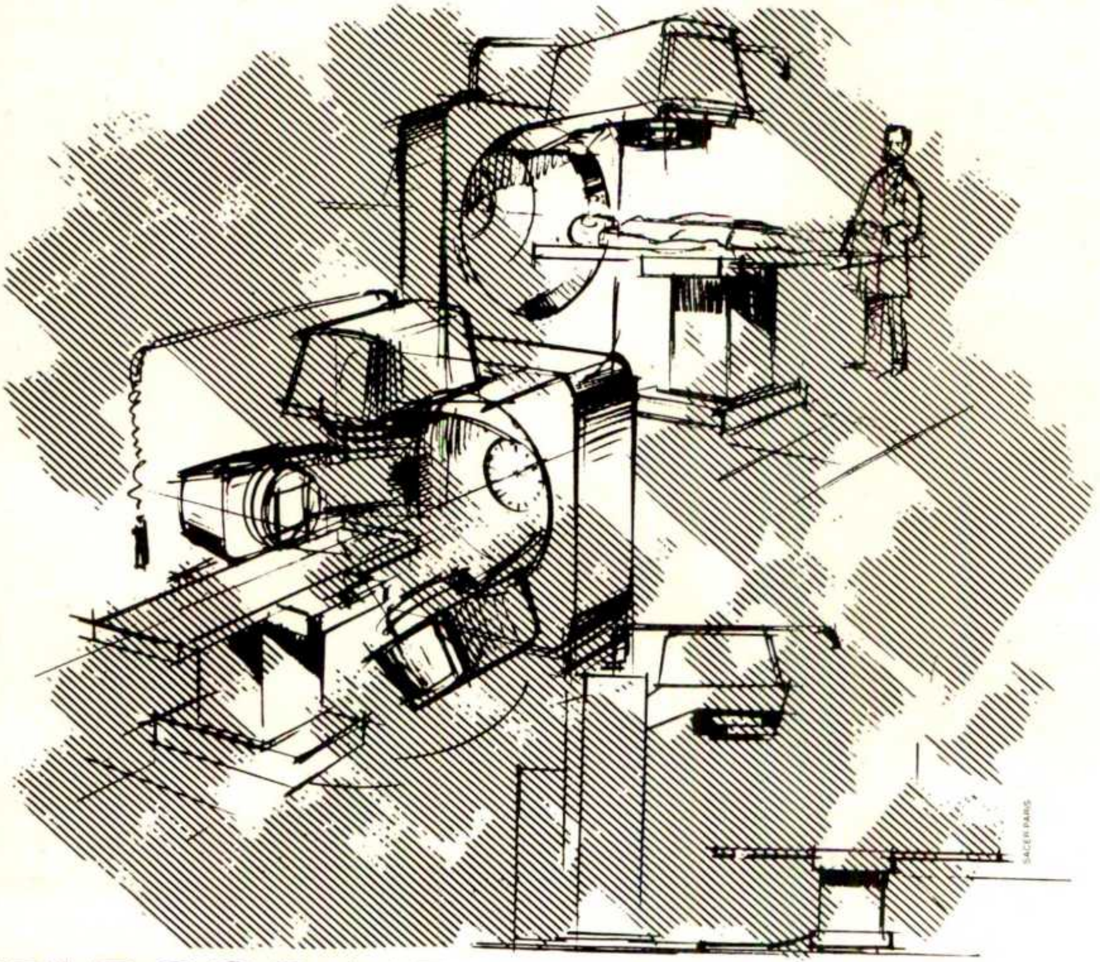
Name
Address
City
Country

Oldelft nv Optische Industrie De Oude Delft

Holland. Postbox 72, 2600 MD Delft
Tel. (015) 14 59 49, telex 38011

U.S.A. Fairfax, Virginia 22030
2735 Dorr Avenue, Tel. (703) 573 7020, telex 089-2759

A new design
...a new technology
yet easy to use and reliable



TELECOBALT
ALCYON
from
CGR

The Alcyon unit features easy installation (no floor pit required), easy servicing and easy exchange of sourcehead. It has 8,000 Rhm capacity, isocentric couch and is very competitively priced. The Alcyon fully complies with R.A.S.M.P. 75.

Full details of this and other treatment linacs from:
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166
Branches at Bristol, Cambridge, Edinburgh, Glasgow,
Manchester, Nottingham.

SHIMADZU MEETS CUSTOMER DEMANDS THROUGH INNOVATIVE ENGINEERING
MOBILE X-RAY IMAGE INTENSIFIER
WHA-10

High quality image ....
- 0.4mm focus x-ray tube
- Image Brightness Stabilizer

High output ....
- Square full-wave rectification x-ray generator

Less x-ray radiation ....
- Video memory
- Motor driven collimator

Simple operation ....
- Radiographic condition memory (Optional)

Free access to patient ....
- Large C-arm steering handle

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Dusseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D.
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

A cup above the rest...

*Proven results.
Just add water and shake.

E-Z-EM®

*Assessment of the Double Contrast Barium Meal: Method and Application. *Lintott et al. Clin. Radiol. (1978) 29, 313—321*

*A new method for studying barium sulphate contrast media *in vitro*. Some factors contributing to the visualization of areae gastricae By Pekka Virkkunen and Minna Retulainen *1980, British Journal of Radiology, 53, 765—769.*

Full details from:

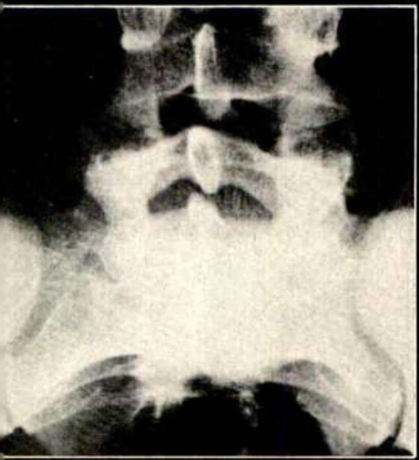
Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151

PL/1665/0003

Produced by E-Z-EM Ltd London

THE 3M TRIMAX SYSTEM:

THREE WAYS BETTER



1. Finer diagnostic quality.

The gadolinium oxysulphide formulation used exclusively by the 3M Trimax System ensures:

a) better definition from this high efficiency phosphor
b) less graininess from a finer, more regular grain structure
c) better image characteristics by reduced probability of scatter.

2. Less exposure time.

The Trimax System is faster - up to 90% faster than conventional systems. This means:

a) less radiation dosage,
b) less chance of patient movement,
c) greater use of fine focus.

3. Longer operating life.

Trimax screens, the first of which wer introduced in 1974, have yet to show any loss of speed.

That's why they all come with an exclusive 7-year guarantee against loss of speed.

That's why replacement ceases to be a factor with the Trimax System.

When it comes to rare-earth x-ray systems, there's only one which offers a fully comprehensive range of screens and films, designed to outperform all the others on the three most critical parameters of: diagnostic quality, radiation dosage and ong-term economy.

3M Trimax System. The most versatile, comprehensive and durable rare-earth system available. Specify it with confidence.

For further information about the Trimax System from 3M - the leaders in rare-earth phosphor technology - contact: Alan Budge, X-Ray Products, 3M United Kingdom Ltd, 3M House, PO Box 1, Bracknell Berks, RG12 1JU. Telephone Bracknell (0344) 58458.

3M and Trimax are trade mar

SIEMENS

Vhatever your
riority in
Jltrasonics...

**utomatic, Computer-controlled Dynamic
nd High Resolution Static B-scanning**

e Sonography System RA-1 diagnostic ultra-sound
anner uses sophisticated, computer-controlled
age processing to achieve superior image resolution.
e advanced, state-of-the-art scanheads comprise:
FOV scanheads for multiformat abdominal
anning.
VV scanheads for high frame-rate scanning.
Small parts scanhead, incorporating Doppler with
ectral Analysis, for superficial vessel and organ studies,
neonatal and paediatric scanning.
e modular design guards against obsolescence whilst
rmitting expansion and the ability to retrofit new
aging techniques as they are developed.

**Universal Computer-controlled
High Resolution Static B-scanning**

The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

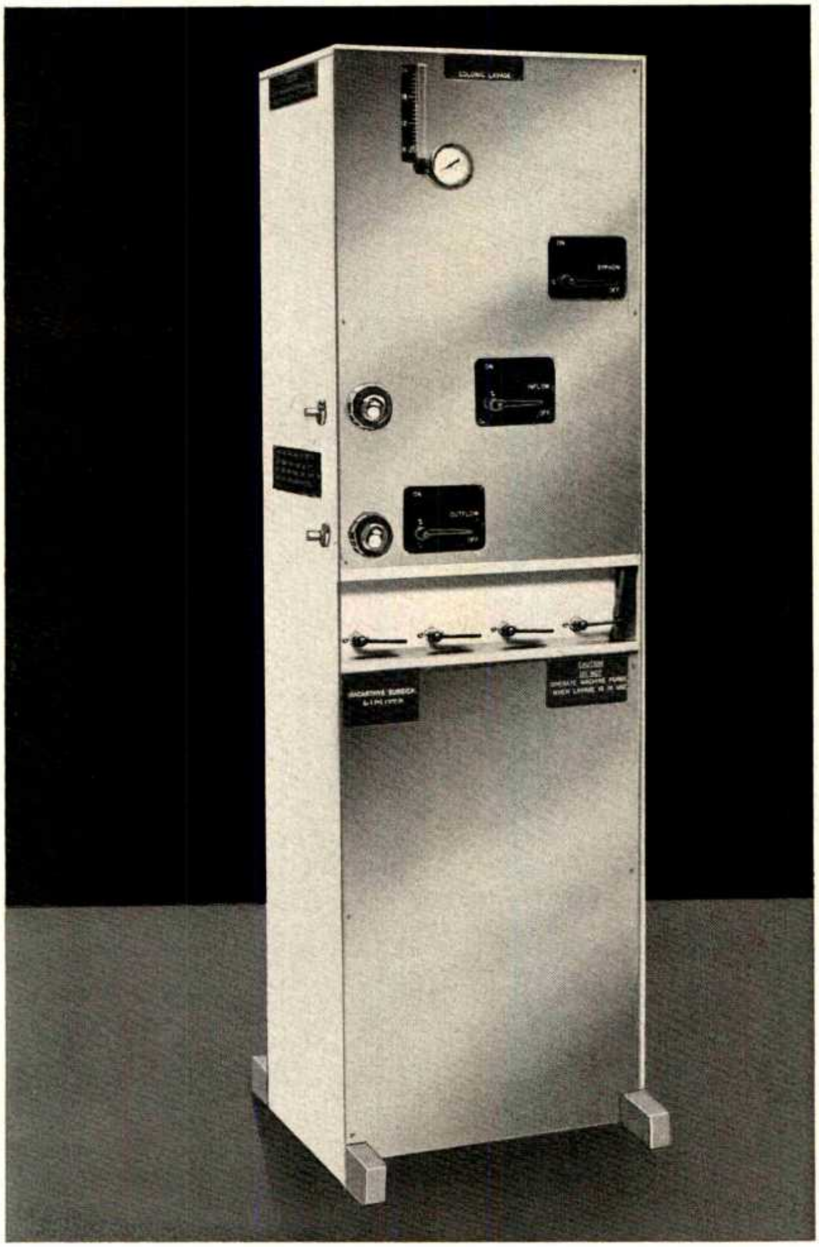
❋ Wide range of transducers ❋ Image Process Functions
❋ Area, Circumference and Volume measurements.
❋ Obstetrics measurement facility ❋ Floppy disc interface

Future improvements to the image processing may be incorporated due to the flexible computer software.

Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner.
For full details write to: Siemens Medical Group, Siemens Limited,
Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691.

..Siemens gives you the choice!

HENDERSON
COLONIC LAVAGE UNIT



The Henderson Colonic Lavage provides a simple, effective and safe apparatus for washing out the large intestine and the terminal ileum of the small bowel.

The Henderson Colonic Lavage is indicated for patient preparation prior to surgery or radiography.

An important feature of this machine is, that as fluid is withdrawn from the patient, air is admitted to maintain the full lumen of the bowel, permitting complete fluid evacuation and assisting further faecal removal.

Macarthys Surgical Ltd

DAGENHAM
Selinas Lane
Dagenham, Essex RM8 1QD
Tel.: 01-593 7511

BIRMINGHAM
Unit 25/28
Edgebaston Shopping Centre
Hagley Road
Birmingham B16 8SH
Tel.: 021-454 6713

GLASGOW
301-3 Glentanar Road
Balmore Industrial Estate
Glasgow G22 7UG
Tel.: 041-336-8782

LIVERPOOL
201-3 London Road
Liverpool L3 8JS
Tel.: 051-207-1348

MANCHESTER
Precinct Centre
Oxford Road
Manchester M13 9GS
Tel.: 061-273-6754/5

Clinical and Experimental Applications of Krypton 81m

Edited by J. P. Lavender

British Institute of Radiology
Special Report 15

This work is composed of papers presented at an International Meeting held in June 1977 concerned with a new physiological tool; the use of a very short-lived radioactive gas krypton 81m.

Krypton 81m is a noble gas with a 13 second half life available from a portable generator with a half life of 4½ hours. Although known for a number of years it has only been used with any frequency by physiologists and clinicians since 1975.

The first section of the book deals with the production of the parent isotope rubidium 81 and the design of generators. The second section comprises a series of papers concerned with the use of the equilibrium image as both a picture and a measure of regional lung ventilation and perfusion. It also outlines problems of deriving absolute values of lung function. In the third section, papers illustrate the use of krypton 81m as a clinical tool in the diagnosis of pulmonary embolic disease and other pulmonary diseases and compare such information with that obtained from the more familiar xenon 133. In the last section the use of intra-arterial krypton as a marker of regional myocardial and cerebral blood flow is discussed. This technique, which has been most highly developed in the case of the myocardium, allows detailed images of the myocardial perfusion to be recorded. Perhaps its clearest application is in following rapid changes of regional myocardial perfusion in response to transient ischaemia, stress and drugs.

The discussion following each paper allows an assessment of the value and place of this new technique.

Price £12

ISBN 0 905749 01 4
ISSN 0306–2120

Orders to:

Publications
The British Institute of Radiology
36 Portland Place
London W1N 3DG

or your local bookseller.

SOUTH AFRICA

JUNIOR RADIOLOGIST

required for busy 260 bedded private hospital in

JOHANNESBURG

British trained with DMRD qualification. Salary R48000 p.a. (approx £28,235). Air fare paid. Free accommodation. Car provided. Low cost of living.

To apply contact: **Sue Bentley, Medic International Limited, 49 Camden High Street, London NW1.**

Fellowship in Brachytherapy

Two positions available July 1, 1982,
with research and O.R. opportunities,
emphasizing lung and prostrate.
Three years of radiotherapy training
and VQE required.

Apply: Dr. Beryl McCormick,
Memorial Sloan-Kettering Cancer Center,
NYC, NY 10021.

University of the Witwatersrand, Johannesburg
and
Johannesburg Hospital,
Transvaal Department of Hospital Services

PROFESSOR OF RADIATION THERAPY/
CHIEF RADIATION THERAPIST

Applications are invited for the post of Professor of Radiation Therapy and Chief Radiation Therapist at the Johannesburg Hospital.

The appointee should be registrable with the South African Medical and Dental Council as a specialist in Radiotherapy.

Duties are to be assumed on 1 January 1982, or as soon as possible thereafter.

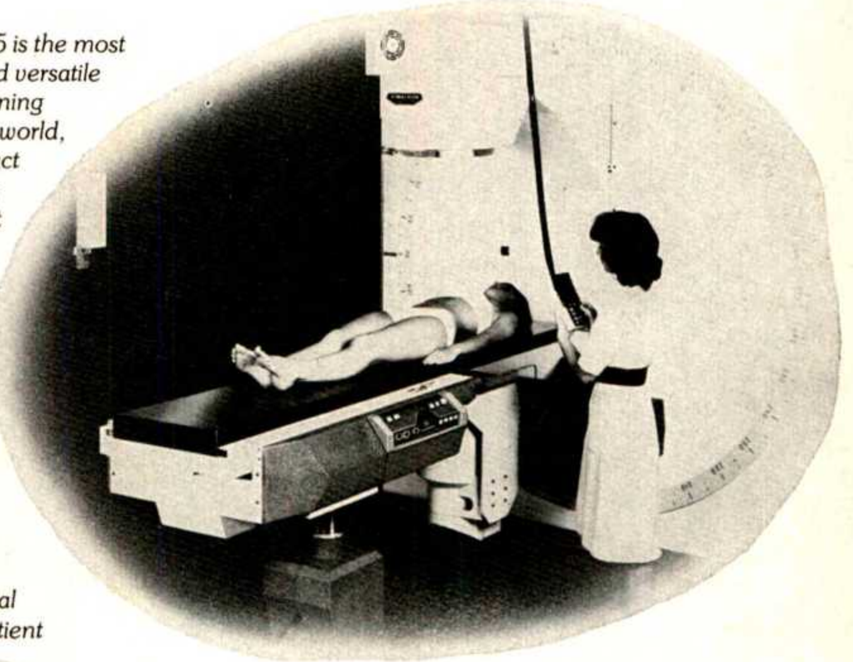
Salary will be R29190 per annum (fixed) and an additional non-pensionable allowance of R8 400 per annum is payable for approved additional duties performed.

Interested persons are invited to obtain the information sheet relating to this post from the London Representative, University of the Witwatersrand, Chichester House, 278 High Holborn, London WC1V 7HE, or from the Registrar (Staffing), University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa 2001, with whom applications should be lodged by 23 October 1981.

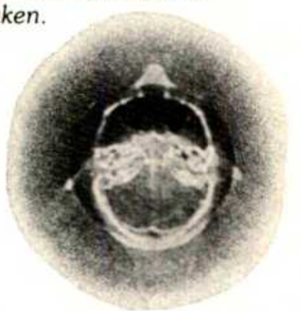
T E M

Ximatron 5 Treatment Planning Simulator

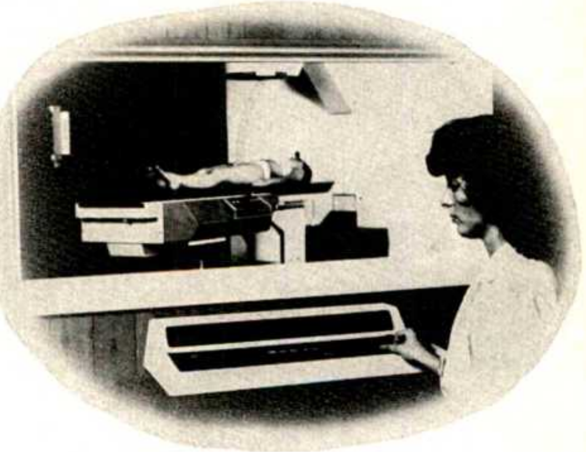
The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.



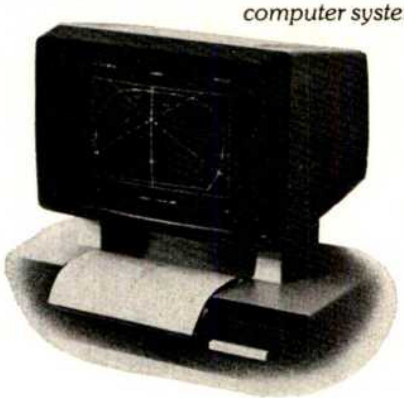
Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.



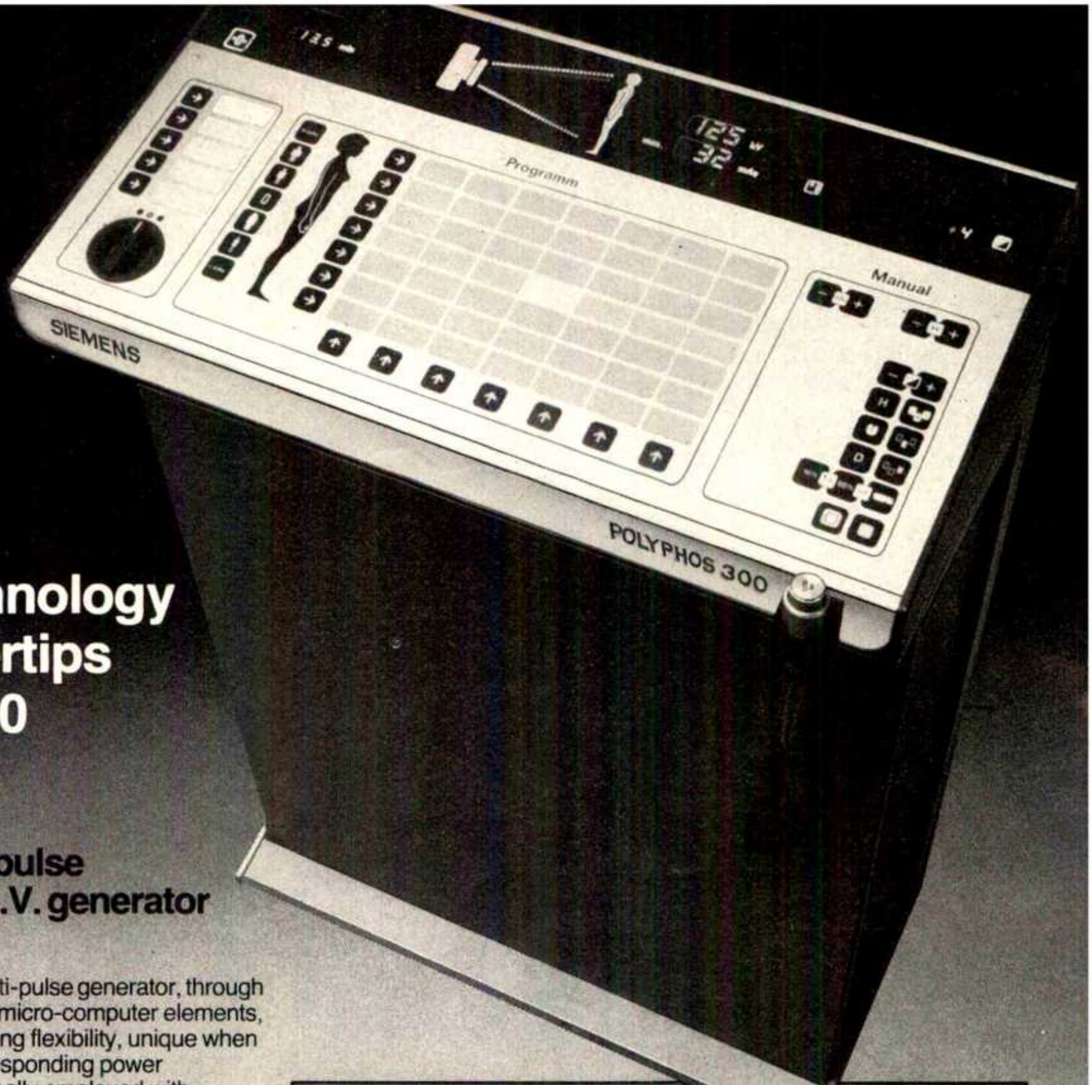
The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY

IEMENS



lexible technology
t your fingertips
olyphos 300

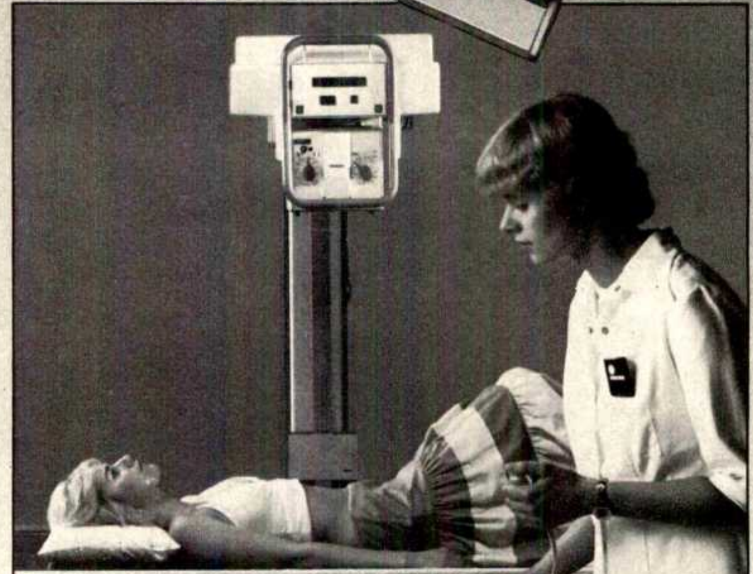
ingle-tank multi-pulse
iagnostic X-ray H.V. generator
30KW

The POLYPHOS 300 multi-pulse generator, through
e utilisation of ultra-modern micro-computer elements,
ers a high degree of operating flexibility, unique when
mpared with units of a corresponding power
assification. It can be universally employed with
agnostic X-ray examination units for radiography,
oroscopy or planigraphy.

The multiprogramming system (organ related
posure technique) enables any freely selectable
posure parameter to be incorporated into an organ-
lated program, by the operation of a single button.

atures include:
Highly compact design, requiring minimum installation area.
Single-tube unit utilizing medium frequency converter technology.
Rapid high-voltage and tube current regulation during exposure.
Short exposure times.
Continuously falling load.
Up-to-the-minute technology, with micro-computer elements.
Smooth control panel with touch buttons.
Flexible extension system.
High dose yield as a result of the multipulse configuration.

r full details contact: Siemens Medical Division,
emens Limited, Siemens House, Windmill Road,
nbury-on-Thames, Middlesex TW16 7HS.
l: Sunbury-on-Thames (09327) 85691.
lex: 8951091.



iemens – X-ray innovation is our business

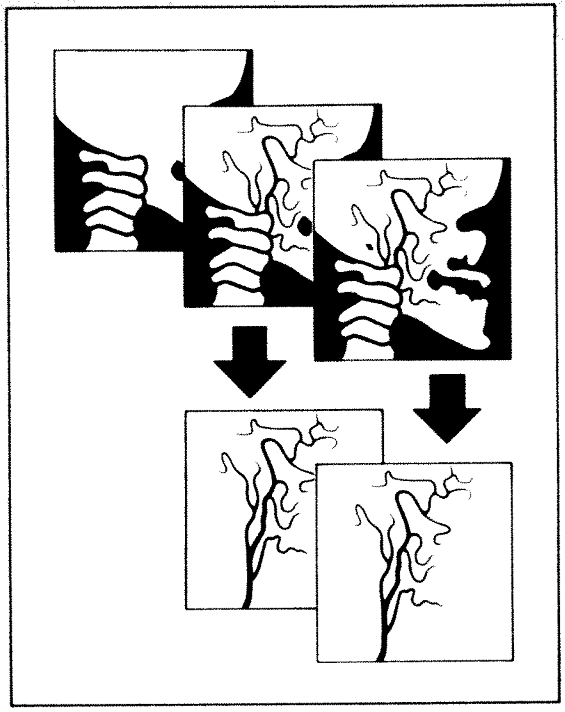
IT'S YOUR RESULTS THAT MATTER.

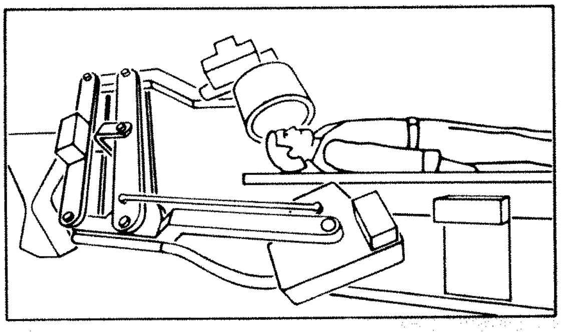
Digital vascular imaging.

DVI is an advanced digital processing system for performing intravenous angiography with real-time image subtraction.

DVI provides angiographic-calibre information achieved by IV contrast administration and is

- relatively non-invasive
- a low risk technique
- quick and simple
- easy to perform:
  - ○ no catheter manipulation
  - ○ no sterile technique
  - ○ no femoral puncture or cutdown
  - ○ no post-procedure patient monitoring
- an ideal outpatient procedure requiring no hospitalisation
- cost effective





DVI's clinical applications include:

- asymptomatic vascular disease screening
- evaluation of the high risk patient
- post-surgical evaluation and follow up
- an adjunct to both conventional and interventional angiography
- a "first order" diagnostic tool in lieu of conventional angiography

Because of DVI's unique subtraction and enhancement capabilities, other potential applications most certainly will develop with increased clinical usage.

PHILIPS

Medical Systems

For detailed information write to Philips Medical Systems, Kelvin House 63/75 Glenthorne Road, Hammersmith, London W6 0LJ.

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY
C. V.

"EVERYTHING X-RAY"

THE ELEVENTH (GOLDEN) EDITION

Just to remind you, without reprinting here the whole 13-column detailed index, of some of the things included in the above edition of this catalogue, which was first published in 1934:

LYSHOLM grids, Smit grids, protective sheaths, gridded cassettes et cetera.

CASSETTES with intensifying screens, intensifying screens without cassettes, cassette trolleys, cassette holders, cassette chests, cassette tunnels, cassette hatches et cetera.

X-RAY FILM VIEWERS of all makes and types, horizontals, splash-proofs, gas-tights, lecture units, transparency viewers and slide holders, wet film attachments et cetera.

DARKROOM ACCESSORIES, lamps and filters, film bins, manual processing units, mixing plungers, syphons, drying cabinets, immersion heaters, thermometers, exhaust fans and light-proof grilles et cetera.

FILM MARKERS of all types, light markers, Cellumarks, cassette clips, lead letters, perforators, self-adhesive labels et cetera.

PROTECTIVE ARTICLES, aprons, gloves, gonad and ovary protectors, mobile screens and seats, lead plywood, lead glass, the new clear lead-plastic sheeting et cetera.

PHILIPS 'ULTRA' SCREENS have arrived since publication. Speed and definition are strictly comparable with Ilford Fast Tungstate but prices are 17% to 37% lower.

CUTHBERT ANDREWS

EVERYTHING X-RAY LTD.

5 HIGH STREET, BUSHEY VILLAGE, WATFORD WD2 1BE

Overseas telegrams:
EXRAYZE WATFORD

Telephone:
01-950 2525

Telex:
Evex 925859 Elwood G

1981, *British Journal of Radiology*, 54, 831–849

VOLUME 54 NUMBER 646 OCTOBER 1981

The British Journal of Radiology

Special announcement

Readers please note that as from September 1, 1981, the address of the Editorial Office of *The British Journal of Radiology* will be the new headquarters of The British Institute of Radiology at

36 Portland Place, London W1N 3DG

Telephone 01–580 4189 (Editorial) and 01–580 4085 (Institute). The Advertising Department remains at 24a Litchfield Street, London WC2H 9NX (telephone 01–836 5281).

The noes have it! Do they?

Silvanus Thompson Memorial Lecture, February 18, 1981

By John Mallard, D.Sc., F.Inst.P., F.I.E.E., F.R.C.Path., F.R.S.E.

Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen, Scotland

(*Received March 1981*)

I was shattered to be invited to give this Memorial Lecture, so much so that it was a long time before my little grey cells could summon up the courage to accept and fix the date. My feelings of panic were made worse when I saw the list of earlier lecturers—a list which includes Rutherford, Lodge, de Broglie, J. J. Thomson, the Braggs, father and son, Eddington—great names which tower like skyscrapers in the history of modern physics; and then, more recently, great people whom I have met and have had the privilege of talking to and learning from—Russ, Sievert, Stead, Gray, Mayneord, Mitchell, Lamerton, Johns, Hounsfield. However, we are now into the 1980s and I can only conclude that the BIR Council must be TV buffs and must have asked me because my initials are J. R. and I come from a far-distant oil city.

This is the 59th lecture in memory of Silvanus Phillips Thompson (Fig. 1). He was a brilliant physicist, a mathematician and an engineer. It is forgotten that he was the British discoverer of radioactivity. It is clear from Silvanus's biography (Thompson and Thompson, 1920) that during February 1896—the month after the report in the Lancet of Röntgen's photographic action of X rays—Thompson found a photographic action from uranium salts, even through aluminium sheet which was impervious to X rays. He wrote to the then President of the Royal Society on February 26th, 1896, who encouraged him to publish his results. Thompson's paper was not read until June 6th but by then Becquerel had published an account of his work, of which a preliminary account had appeared in *Comptes Rendus* for February 24—only two days

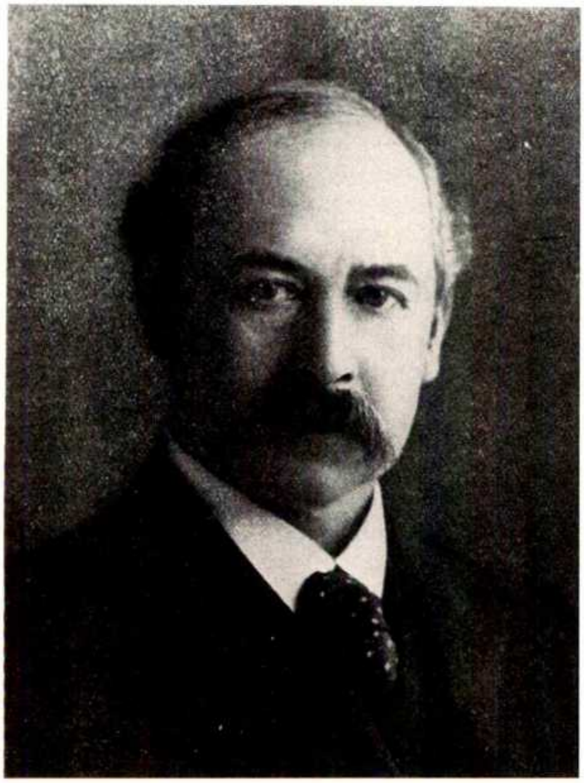
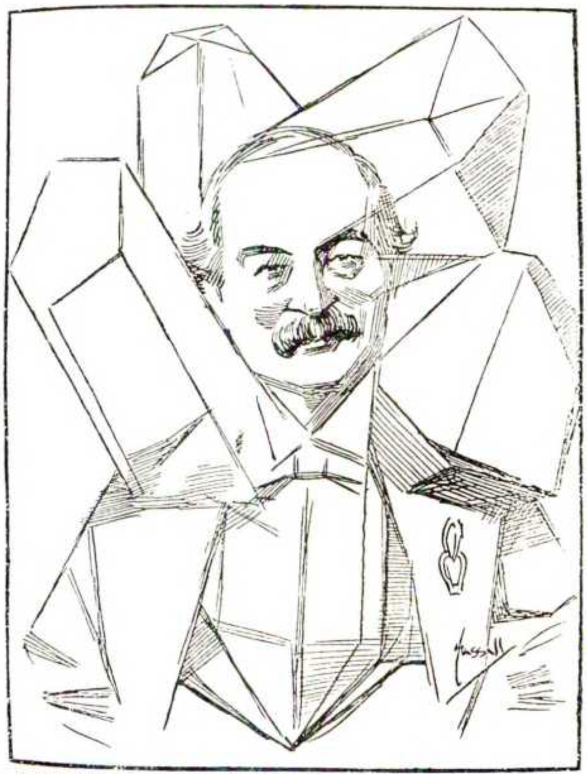


FIG. 1.
Silvanus Phillips Thompson (Thompson and Thompson, 1920).



A Many Sided Crystal. Very rare. The property of Ye Sette of Odd Volumes. NOT a Cubist Portrait.

Brother Magnetizer.
FIG. 2.
Caricature of Silvanus Thompson (Thompson and Thompson, 1980).

before Silvanus's letter. There's a moral here, I suppose, "Publish and be damned", but from now on I am going to refer to the new SI unit of radioactivity as being the Becquerel-Thompson, in the same way as we say Geiger-Müller tubes. Maybe the longer name will help to make this very small unit seem bigger.

Thompson's interests were wide and his contributions were many. They include crystallography and gems—hence this caricature (Fig. 2) drawn by one of his friends during a brilliant lecture by him at the Royal Institution. He was interested in magnetism—he translated his own personal copy of the manuscript of the first recorded scientific investigation of magnetism in the 13th century by Peter the Pilgrim, a wandering soldier of fortune: there are only about 20 copies in existence—and he personally decorated the printed copies of his translation. He was also an authority on luminescence, optics and sound. In my more imaginative moments, I like to think that he would be interested to hear about the uses to which these various physical phenomena are being put today, which is what I intend to talk about. There are now so many new uses of them bubbling-up at this time that I thought that I would break away from the major tradition of this Institute and these Memorial Lectures, and talk about the potential uses in medicine of non-ionizing radiations and magnetism.

TELE-DIAPHANOGRAPHY

There is much interest in the early detection of breast cancer. In America one woman in 11 gets the disease (Strax, 1980), and if it is detected at a very early stage a real cure is feasible. Whilst prevention is the ideal goal, the next best line of attack is to detect it in apparently-well women. This means a mass screening procedure. It is very important to realize that a mass screening test is not intended to be diagnostic—it is helpful if it is, but its real purpose is to sort out those who may benefit from more exhaustive diagnostic investigations.

It is now clear that palpation and X-ray mammography offer the most reliable diagnosis at present but, due to the radiation dose, there is a small but finite risk of inducing cancer—an increased risk of

1% per rad (NCRP 66). Strenuous attempts over the last decade have been made to reduce this dose and the examination can now be done with a mid-plane dose of 0.5 cGy (rad) down to 0.05 cGy (NCRP 66). Whilst this is acceptable for diagnosis, if this exposure were to be repeated every year or so to well women as a screening test, the risk would still be finite. This fact has, of course, led to considerable interest in other techniques where the risks are believed to be negligible or zero; for example, ultrasound and infrared thermography. In addition, the more techniques that are used for screening or diagnosis, the higher the overall accuracy.

In thermography one detects the increased infrared emission arising from an increased tumour temperature. The extra heat is lost mainly by increased blood flow in dilated superficial vessels. Thermography has been disappointing as a screening procedure used in isolation, due to a relatively high false-positive rate. This arises because often superficial blood vessels are not always above a tumour; non-malignant diseases may also increase the temperature; the contraceptive pill gives abnormal patterns; and bilateral disease is difficult because there is not a normal breast for comparison. The real problem is finding the early small tumours.

In Aberdeen, equipment to shine light through the breast (diaphanography)* is being modified and improved (Watmough, 1981). The torch is a cooled bright light source and the examination is carried out, after dark adaptation, in a completely darkened room. The idea goes back a long way (Cutler, 1929; Wilson, 1936). The basic idea seems to have had wide general use because simple devices were available for other applications by general practitioners in 1936 (Bailey)†. Nevertheless, for breast examination the method lay largely unused until it was reintroduced by Ohlsson *et al.* (1977).

The physical phenomenon which is being used is the transmission of light through soft tissues and there is confusion in the literature. Figure 3 shows results of measurements (Hardy and Muschenheim, 1934; Hardy *et al.*, 1956). One shows a transmission of 1% maximum through a millimetre of white breast skin and subcutaneous tissue, whilst the later work is about 25%. However, peak transmission at about 1 μm is common to both. Fortunately, the radiation emission curves from tungsten lamps above 2500 K shows a peak at 1 μm. The present commercial apparatus consists of the torch, which also has a flash exposure; a transmission colour photograph is taken with infrared sensitive film. In general, carcinomata are seen as dark. There is some evidence that the tumour tissue itself absorbs more light, and in addition there is a contribution from the increased absorption of light by the blood in the venous dilation associated with the tumours. Benign cysts show as more transparent.

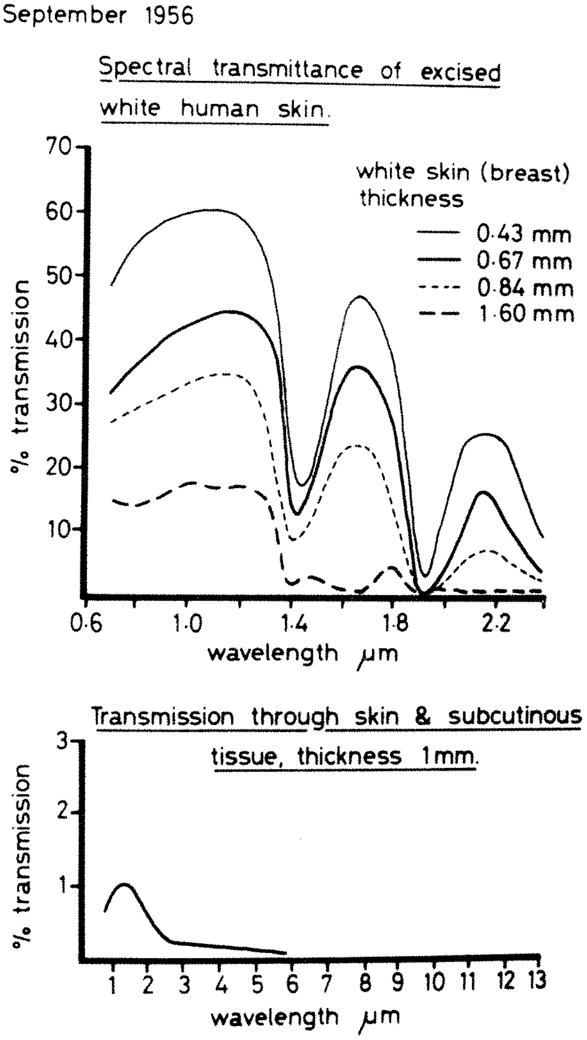


FIG. 3.

Spectral transmittance of skin and tissue. Upper curves, Hardy *et al.* (1956). Lower curve, Hardy and Muschenheim (1934).

In a small preliminary series (Hussey *et al.*, 1981) carried out in Aberdeen using the commercial prototype, diaphanography seems as accurate as mammography for the detection of carcinoma (Table I). One carcinoma missed by mammography

---

*Sinus Medical Equipment AB, Norrlardsgaten 31–33, 11143 Stockholm, Sweden.

†Genito-Urinary Manufacturing Co. Ltd., 3 Plympton Street, London NW8.

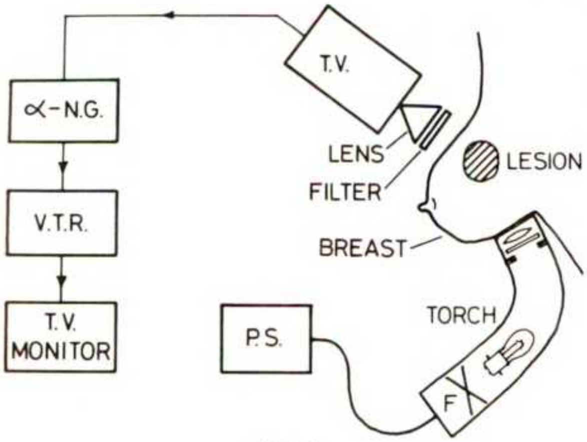


Fig. 4.

Tele-diaphanography system using TV camera and display for immediate interpretation (after Watmough, 1981). British Patent Application No. 8104279 applies.

was picked up by diaphanography, and *vice versa*. In this Aberdeen series, no lesions were less than 8 mm, but smaller ones down to 5 mm have been reported from the Swedish series. The technique looks useful, but needs improvement to find smaller lesions and to make it a quicker examination. A system using a TV camera with a zoom lens and filter is now being used, the output passing through an alpha-numeric generator to record the patient's data, a video recorder and a monochrome monitor (Fig. 4). The image is immediately available for interpretation.

Experiments with an appropriate phantom (Watmough, 1981) show that 6 mm diameter lesions are clearly visible using the appropriate aperture of the light source to reduce scatter. Figure 5 shows a carcinoma detected by this system. The use of a colour TV system will exploit the colour changes observed with different disease states.

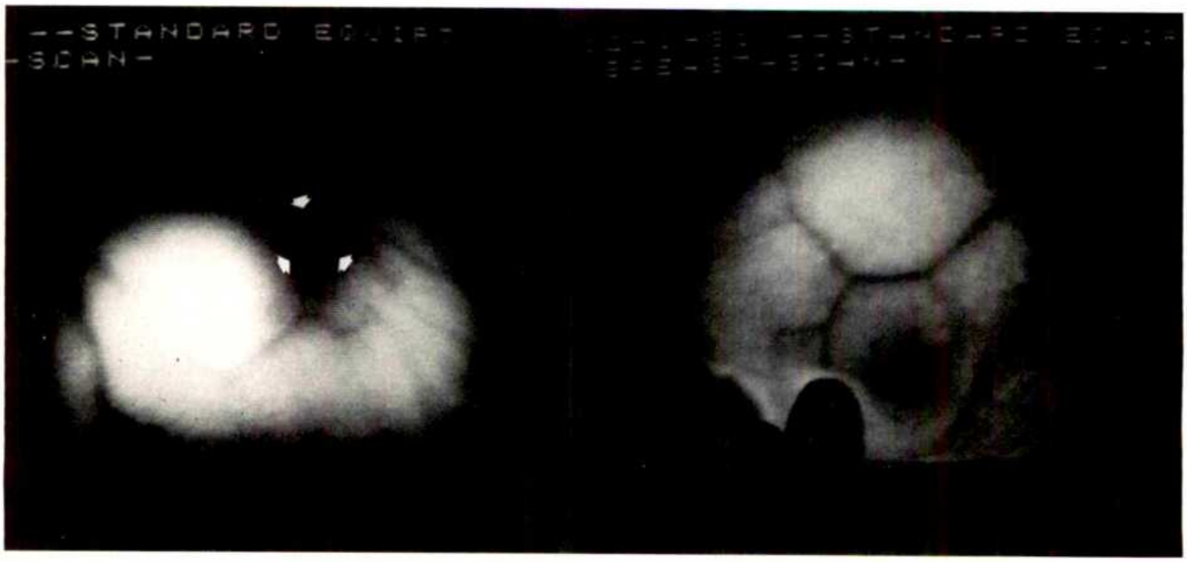


Fig. 5.

Carcinoma of the breast (indicated by arrows) demonstrated by tele-diaphanography. The normal contralateral breast shows the dark shadow of the nipple. British Patent Application No. 8104279 applies.

TABLE I

Mammography, diaphanography and thermography

	Normal		Simple lesions		Carcinoma	
	True negative	False positive	True positive	False negative	True positive	False negative
Mammography	51	3	60	3	12	1
Diaphanography	51	2	48	12	12	1
Thermography	45	6			7	5

Positives biopsy-confirmed: smallest 8 mm.

Ultrasound Hyperthermia

Ultrasound is used at low power levels for diagnostic imaging, but can also be used at power levels 10000 to 100000 times greater to deposit sufficient heat in tissue to increase its temperature. This has been, and still is, used in physical medicine for the relief of pain in soft tissue injuries, the acceleration of wound healing and the reduction of scar-tissue formation. It is also used for the destruction of tissue, such as warts and middle ear structures in Menière's disease. There is now rapidly growing interest in using ultrasound for a form of tumour therapy by hyperthermia.

There are many physical effects of ultrasound such as cavitation, streaming, disruption of cellular membranes and even induced oscillation of cellular membranes (Watmough *et al.*, 1980). It may be that with more knowledge of them, these effects can be used to enhance tumour tissue damage but, for the moment, it would seem that the thermal effects predominate and give by far the greatest biological damage (Lele, 1975).

Experimentation over the years has led to the conclusion that one needs to raise the temperature of the tissue to between 42° and 45°C for many hours to obtain a breakdown of cellular biochemistry leading to a local reactive hyperaemia. This leads to a local coagulated necrotic lesion without haemorrhage, so that the chance of metastatic spread is very small. There is some experimental evidence of failure to induce metastases by irradiating intraperitoneal tumours with ultrasound (*ibid.*). There is also evidence of cancer tissue being more sensitive to heat, this depending upon tumour type, but only between 42° and 45°C. At lower temperatures there are reports of stimulated growth and at higher temperatures the difference in heat sensitivity between tumour and normal disappears (Short and Turner, 1980). So in the clinical situation one wants to have the tumour at a higher temperature than the surrounding tissue, in order to spare the normal tissue unnecessary damage, and for some tumours a heating to higher than 45°C for 30 minutes or more seems desirable. Bowl-shaped transducers can be used to generate a focused beam and direct it to the tumour (Lele, 1979).

Work is in progress in Aberdeen to evolve a practical system for ultrasound hyperthermia. Calculations have been carried out to try to determine the optimum irradiation from the physical point of view (Hynynen *et al.*, 1981a). Figure 6A shows that the focus is deepest at 1 MHz, whatever the size of the transducer. At lower frequencies the focusing effect is not good. At higher frequencies it is better but there is more absorption of the ultrasound, so the focus itself cannot be thrown so deep. Experiments demonstrating the heating effect by irradiating a gelatin phantom with a focused transducer have been carried out. An infrared thermograph has been used to display the heating effect. Focal hot spots in agreement with the calculations have been observed (Fig. 7). However, the use of a gelatin model is not good because the attenuation of ultrasound in gelatin is much lower than that in normal tissue. Figure 6B

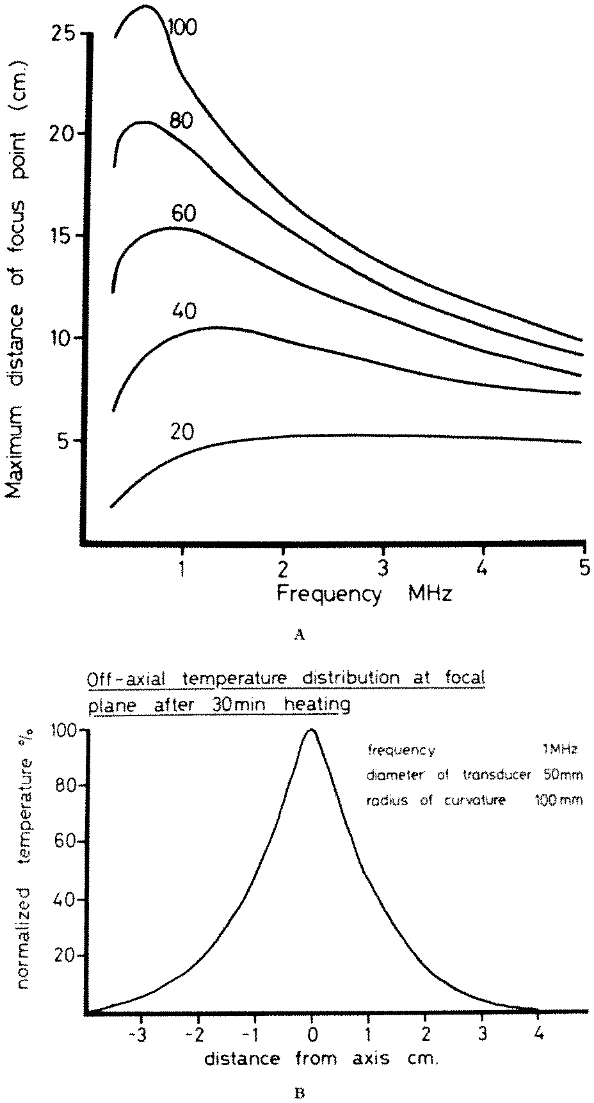


Fig. 6.

(A) Calculated maximum distance of focal point of spherical bowl-shaped ultrasound transducers of diameter from 20 to 100 mm as a function of frequency. (Hynynen *et al.*, 1981a).

(B) Off-axis distribution of temperature in the focal plane of a focused ultrasound transducer (from Hynynen *et al.*, 1981b).

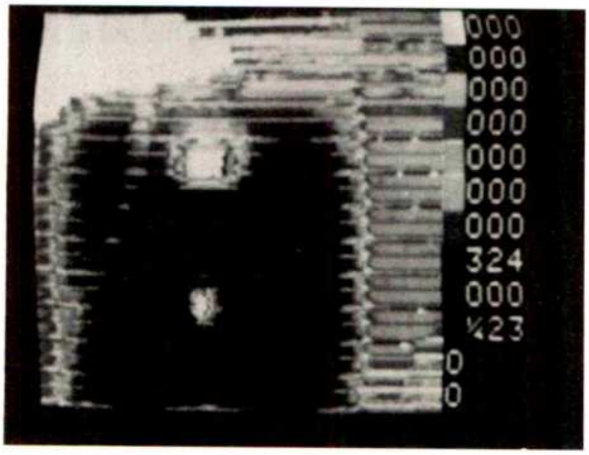


FIG. 7.

The focal hot spot from a 1 MHz ultrasound transducer of 38 mm diameter and radius of curvature 70 mm. An infra-red thermograph has been used to demonstrate the temperature changes. The transducer itself is seen at the top. (Hynynen *et al.*, 1981b).

TABLE II

SCHEME FOR TREATING PATIENTS WITH ULTRASOUND

Temperature:	Surrounding tissue ⩽45° Tumour⩾45°
Time:	30 min
Equipment:	Frequency 1 MHz Focused transducer: spherical and/or many overlapping fields 3-dimensional movement of the transducer to improve uniform heating in the tumour Computer model to predict temperature distribution during treatment 2–3 invasive thermocouple probes (diameter <0.1 mm) to calibrate computer model for each patient
Treatment can be repeated as many times as necessary if X-irradiation has not been used.	
Irradiation:	If used, 3–4 h after hyperthermia treatment (Tumour cells more sensitive to radiation than normal cells at this time)

shows the width of the temperature distribution in a uniform muscle, allowing for the thermal conduction of heat away from the irradiated volume. At 1 cm from the focus, the temperature elevation is just below one half of that at the focus.

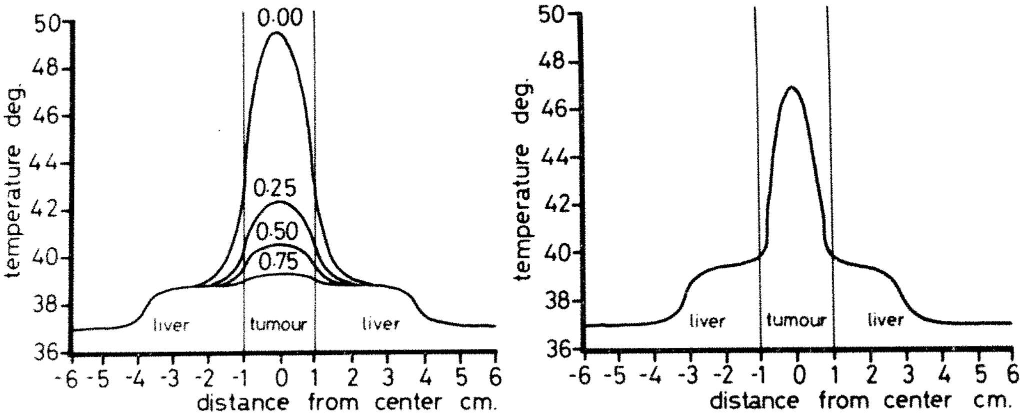
However, of course, the patient is not just a block of gelatin or uniformly made of muscle. A one-dimensional computer model has been developed which allows for such *in-vivo* factors as the blood flow in the tumour, vasodilation, different sizes of tumour, and the different ultrasound absorptions in different tissues (Hynyen *et al.*, 1981b). The model assumes a uniform ultrasound irradiation stretching 3.5 cm on both sides of the centre. The blood flow carries away the heat from the region being heated and 4 to 5 times higher power input is needed than when there is no blood flow. Blood flow in tumours varies greatly: the rapidly growing periphery is usually well perfused, but the centre can be necrotic. The average value in the tumour core is only 1% to 30% of the blood flow in the host tissue, which makes it easier to heat the core. Figure 8A shows this clearly from the computer model—as the tumour-core blood-flow is smaller, so the temperature achieved is higher. However, the well-perfused periphery has a greater blood flow than that of the host tissue and therefore does not reach such a high temperature (Fig. 8B). To increase the concentration of the ultrasound energy to the outer part, more than one irradiating field might be used, as one does in normal X-ray therapy, or alternatively the focus could be moved about over the tumour volume. Another approach would be to treat with radiotherapy or chemotherapy the malignant cells which are still viable after ultrasound hyperthermia.

Another problem *in vivo* is that when tissue is heated the blood vessels dilate and the blood flow increases to take away the unwanted heat. In muscle and fat, the blood flow may increase to ten times higher than normal. However, blood vessels in the necrotic core and even those in the well-perfused front of the tumour cannot do this. The effect of this factor, which increases the temperature rise in tumour relative to host tissue, even in the periphery, is seen in Fig. 8C.

As a result of thermal conduction in tissues the temperature rise in small tumours is lower than in large ones: it is easier to increase the temperature of a large tumour than a small one. Figure 8D shows the effect which would result if tumours had a higher ultrasound absorption coefficient than the host tissue. There is some evidence that this may be so (Kikuchi *et al.*, 1957).

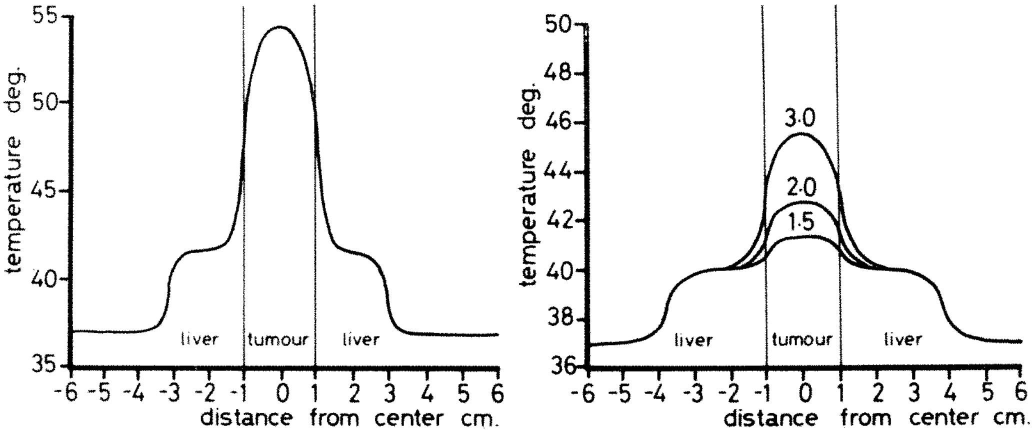
These calculations do not include any beam focusing on the tumour, nor the use of multiple fields or transducer movement to spread the heating. A possible therapy regime is outlined in Table II. Animal experiments are in progress.

The computer model may be used to predict the temperature distribution but some calibration points are needed by measuring the temperature at depth. This is not easy as it is not really practicable to use thermocouples at depth. A non-invasive temperature-measuring device is needed. In addition to



A Reduced tumour core blood flow

B Increased blood flow at tumour periphery



C Vasodilation of host tissue

D Increased tumour absorption coefficient

Fig. 8.

Calculations from a hypothetical computer model of the temperature profile across a 2 cm diameter "tumour" embedded in normal liver tissue irradiated with a uniform beam of ultrasound of 7 cm width centred on the tumour. Four different variables are dealt with separately (Hynynen *et al.*, 1981b).

this problem. possible side effects of the high-intensity ultrasound radiation, such as haemolysis, need to be carefully considered (Wong and Watmough, 1981).

Lyoluminescent Dosimetry

Lyoluminescence is the emission of light when a solid material which has been irradiated is dissolved in a liquid. It was first observed in 1895, shortly after the discovery of X rays. It lay unused, until a few years ago it was rediscovered by Dr. Ettinger and exploited as a new form of radiation dosemeter (Atari *et al.*, 1973).

When a solid is irradiated photoelectric absorption, Compton absorption and pair production cause ionization and some of the freed electrons become trapped somewhere in the energy band structure of the solid crystalline lattice. In inorganic crystals such as common salt they are trapped in impurity centres called F-centres or V-centres. In organic crystals, such as sugars, molecular radicals are formed with an extra unpaired electron. The crystal lattice impedes the movement of these radicals, so the surplus energy from the ionization is stored within the solid crystal lattice. However, as soon as the crystal lattice is brought into contact with a solvent it disintegrates, the radicals are able to move and they combine with one another, the surplus electron energy being then released as photons of light.

The amount of light is proportional to the radiation dose over a very wide range (Fig. 9) (Ettinger *et al.*, 1977). Each sugar is different: mannose dissolves easily in water and gives plenty of light. To measure the light, the irradiated crystals are placed in the hopper of a readout device (Fig. 10) and are dropped into the cell filled with solvent. The light photons emitted are detected by a photomultiplier tube and the integrated output is a measure of total light emission, which in turn is a measure of radiation dose. Carefully calibrated materials provide a 2–3% reproducibility.

The technique is capable of being used for a wide range of application from the very high doses (10^5 cGy (rad) upwards) used for radiation sterilization of medical supplies, for example, to the medium range of doses (10 to 10^4 cGy) for radiotherapy. It is hoped that it can be used for the low range of doses (10^{-1} to 10 cGy) for radiation protection measurements—personnel dosimetry—by adding light sensitizers to the solvent, but this has not fully been achieved yet.

It is now being used for radiotherapy dosimetry in Aberdeen (Ettinger *et al.*, 1980). Small plastic blisters of mannose are sealed, attached to the skin and irradiated during the treatment. The blister is then broken and the sugar dissolved in the readout machine. An automated readout machine is being constructed. The sugar can be kept for several months before there is any significant loss of signal but it must be kept dry. Individual batches need calibrating—they vary by a few per cent only.

The atomic compositions of the sugars are very close to that of tissue (Table III). The average atomic numbers and the numbers of electrons per gram are almost the same, so that Compton, pair production and photoelectric effects will be similar. The dose recorded by the sugar gives a correct indication of the dose delivered to the tissue over a wide range of energies, much closer than other dosimetric methods (Fig. 11). In addition, this applies whatever the radiation—X rays, γ rays, neutrons, heavy ions, pi mesons. For particulate radiations there is no other tissue-equivalent technique available at present, and lyoluminescence is proving to be of great practical usefulness.

Lyoluminescence is really a special form of the general phenomenon of chemiluminescence. With very sensitive light-measuring instruments it can be shown that the inside of the living human body is not

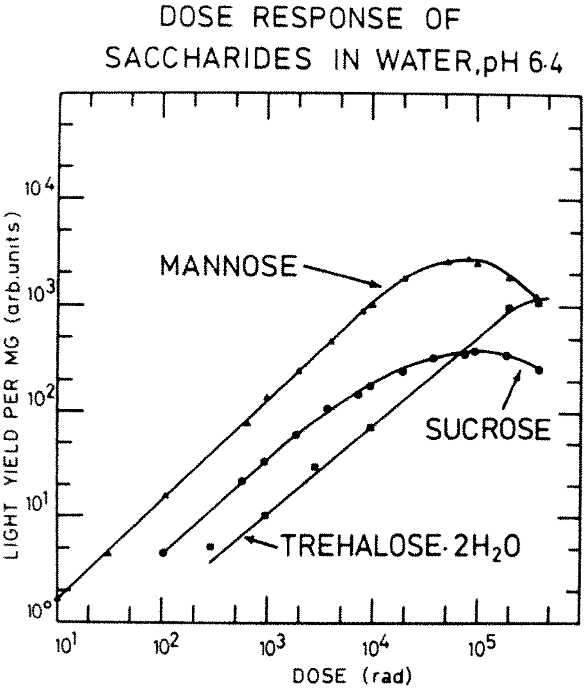


Fig. 9.

The radiation dose response when three irradiated saccharides are dissolved in water (Ettinger *et al.*, 1977).

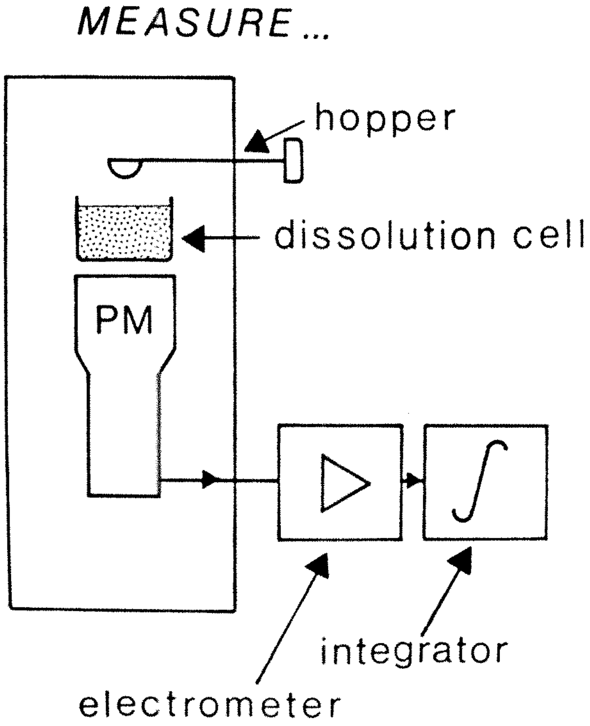


Fig. 10.

The lyoluminescent readout device.

dark but that there is a persistent faint glow which accompanies the chemical reactions of metabolism—bioluminescence (Zhuravlev, 1974). It appears that there is a change in its nature and intensity with some disease states and also with irradiation. It seems fair to say that lyoluminescence not only uses materials of the same composition as the body, but the light emitting processes themselves are closely akin to processes taking place *in vivo*.

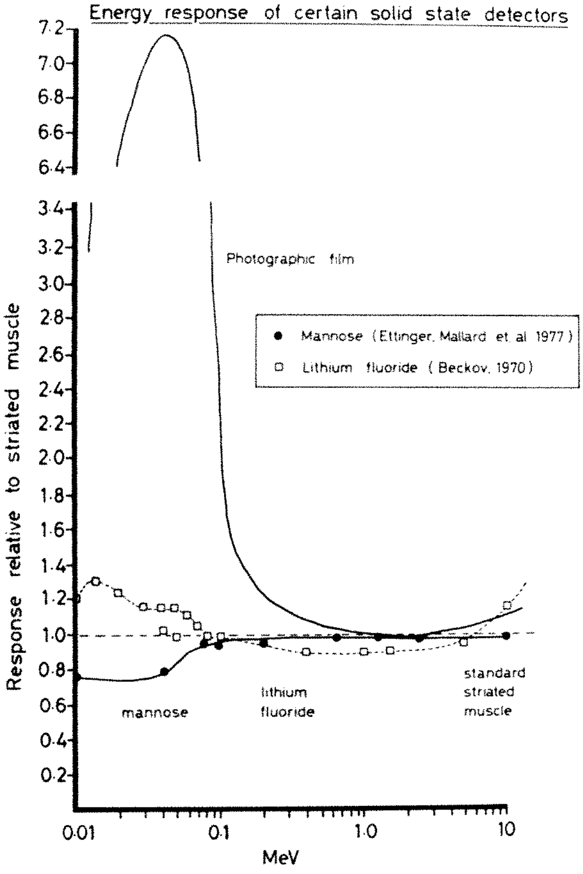


FIG. 11.

Electromagnetic radiation energy response of photographic film, lithium fluoride thermoluminescence and sugar lyoluminescence.

NUCLEAR MAGNETIC RESONANCE IMAGING

For the remainder of this lecture, the ancient problem of water divining is the subject but in the form of finding and imaging water in the body by nuclear magnetic resonance (NMR). The work of the NMR group, which I set up in Aberdeen in 1972, is briefly reviewed. The main designer of the NMR imaging machine, developed over eight years, is Dr. J. M. S. Hutchison, assisted by Dr. R. Sutherland (1975–78), Dr. W. Edelstein (1978–80) and G. Johnson, T. Redpath and R. Selbie, whilst the biological programme has been carried out by Dr. R. Gordon (1972–75), Mrs. R. Ling (1978–81), and in the main by Dr. M. Foster.

Radionuclide imaging or isotope scanning is a way of learning something about a patient, by determining the distribution of a particular atomic nucleus in the body. It is done by detecting the γ-ray photons which the nucleus emits in its radioactive decay. NMR is a new and quite different form of nuclear imaging. It is another way of localizing a particular nucleus in the body, and one does it by detecting the radiofrequency fields which the nuclei radiate after they have been excited in a particular way. No radioactivity is involved at all—merely the natural physical properties of particular atomic nuclei. There are no injections of anything. It is a non-invasive procedure.

NMR spectroscopy has existed since 1945. It has been used almost entirely by physicists, chemists, biologists and biochemists to study atomic and molecular structure. The possibility of using NMR for imaging was not proposed until 1973 (Lauterbur) and this has stimulated considerable activity over the past several years (Hutchison *et al.*, 1974; Kumar *et al.*, 1975; Hinshaw, 1976; Damadian *et al.*, 1977; Mansfield and Pykett, 1978; Hoult, 1979; Mallard *et al.*, 1980; Holland *et al.*, 1980). The potential medical applications of images using parameters

TABLE III

DOSIMETRIC DATA FOR STANDARD MUSCLE AND SOME LYOLUMINESCENT MATERIALS

Material	$\bar{Z}_\tau$	$\bar{Z}_\pi$	No. of electrons per g × 10^{23}	Composition (%)			
				H	C	O	N
Standard muscle	7.2	6.6	3.36	10.2	12.3	72.9	3.5
Glucose. H_2O	7.0	6.4	3.22	7.1	36.4	56.5	—
Mannose	7.0	6.4	3.21	6.7	40.0	53.3	—
Trehalose. $2H_2O$	7.0	6.4	3.22	6.9	38.1	55.0	—
Valine	5.4	5.6	3.29	9.5	51.2	27.3	12.0

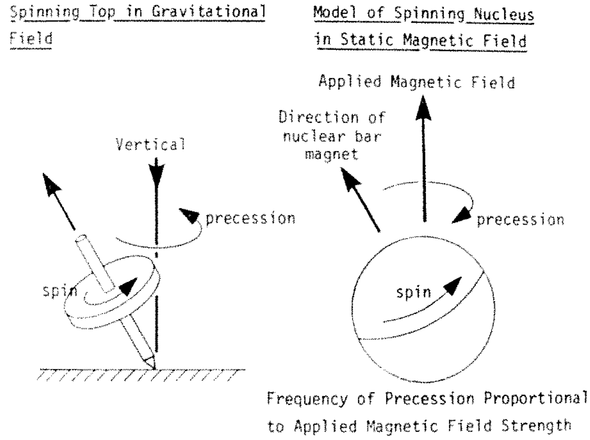

Spinning Top in Gravitational Field
Model of Spinning Nucleus in Static Magnetic Field
Applied Magnetic Field
Direction of nuclear bar magnet
Vertical
precession
precession
spin
spin
Frequency of Precession Proportional to Applied Magnetic Field Strength

Fig. 12.

The analogy between the precession of the nuclear magnetism around an applied magnetic field and the precession of a spinning top around the gravitational field. The frequency of precession is proportional to the applied magnetic field strength.

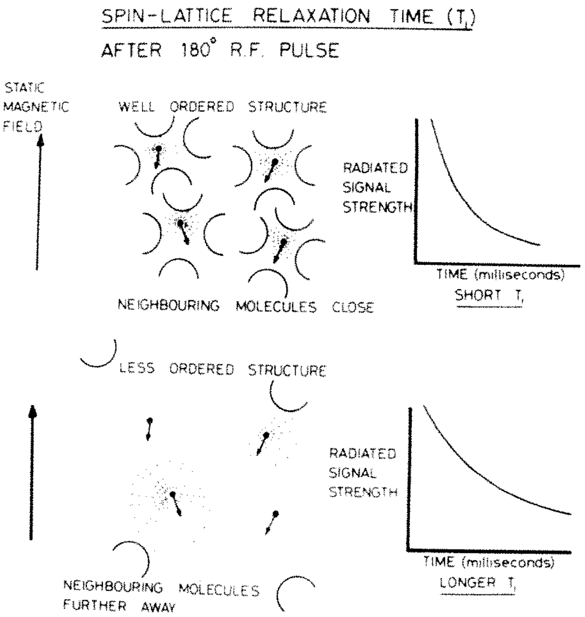


Fig. 13.

Pictorial illustration of the shorter proton spin-lattice relaxation time (T_1) associated with a well-ordered structure of close-by molecules, and the longer (T_1) of a less ordered structure with molecules further away.

measurable by NMR, such as the concentration of hydrogen nuclei (protons) from water in body tissues, or NMR relaxation times of these protons, is considerable. It is the natural body water which is imaged.

The principle of NMR imaging

It helps to go back to childhood days of whip and top (Fig. 12). The top was spun about its axis by the whip but it also wobbled around the vertical, particularly as it slowed down. This wobbling is called a precession. The protons of hydrogen also spin and have an associated magnetic field. They behave like very tiny bar magnets of a definite strength or magnetic moment. If they are placed in a magnetic field, they will line up more or less parallel to that field and will precess around it, as the top does around the vertical gravitational field. The rate or frequency of this precession is proportional to the magnetic field strength in which they are placed.

In nuclear magnetic resonance, one makes use of this precession to study the atomic nuclei and their surroundings by irradiating them with electromagnetic radiation of exactly the same frequency as their precession. At that frequency they absorb energy from the radiation—a resonance absorption—and change their alignment relative to the applied magnetic field. It is even possible, for example, to turn them through 180° and flip them over, if the magnetic field and the appropriate radiation are applied simultaneously as a pulse—a 180° pulse. It is also possible to turn them through 90°—a 90° pulse. The frequency of radiation which has to be used is in the radiofrequency band normally in the region of MHz or tens of MHz.

After a 90° pulse, the nuclei have surplus energy which they radiate to their surroundings at the same resonant frequency. From a sample containing a large number of such nuclei, one by one they are then able to relax back to their original alignment so that the sample reradiates its resonant frequency: this is detected and measured. After a 180° pulse, the surplus nuclear energy is absorbed by the surrounding medium. The length of time needed for this is associated with the environment of the protons because the easier it is for them to pass energy to neighbouring atoms of the lattice of which it is a part, the quicker they can return to their original state; the strength of the signal falls exponentially with time at a rate characteristic of their environment (Fig. 13)—a measurement known as the spin-lattice relaxation time, T_1.

Consider the simple example of two tubes of water lying side by side in a uniform magnetic field (Fig. 14). By irradiating them with electromagnetic waves of the appropriate part of the spectrum and varying the frequency from low to high, one can find the resonant frequency at which the protons of the hydrogen atoms are flipped over. Having found that,

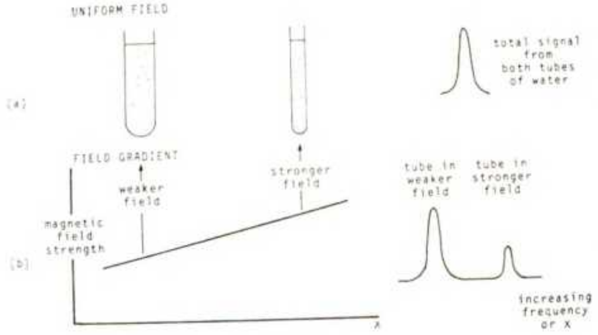


Fig. 14.

The NMR spectrum from two tubes of water placed in (above) a uniform magnetic field and (below) a uniform magnetic field gradient (after Lauterbur (1973) and Foster and Hutchison (1980)).

one can then measure the rate at which the system relaxes back. However, it is not possible to distinguish between the two tubes of water because both have been subject to the same magnetic field and hence have the same resonant frequency; but if one now adds a field gradient to the applied magnetic field, so that the field is stronger on one side than the other, one tube will be in a slightly stronger field than the other and will resonate at a slightly higher frequency. This time, when the frequency of radiation is swept from low to high, the tube positioned in the lower field will absorb energy and then re-emit it at a lower frequency than the other tube (Fig. 14). Thus some information has been obtained on the position of the two tubes in the field, measured from the different frequencies, which can distinguish between them spatially.

If, as in Fig. 14, one tube is bigger than the other, then it will contain more water protons and the size of its signal will be larger, so that from the frequency of the larger signal it is possible to decide which of the tubes is the bigger one. To carry this example further, if one of the tubes were to be filled with water containing a small amount of a substance such as copper sulphate, which enables the protons to relax faster, then by measuring the time taken for the signal to decay at the two different frequencies it is possible to measure the relaxation time of the protons in each tube separately and, from the different decay times, so identify the tube containing copper sulphate.

We have, therefore, the basic information to produce a spatial image of the proton concentration distribution and the relaxation time distribution in a complex sample. The lower spectrum in Fig. 14 is a one-dimensional profile of proton concentration, and by sampling this profile with the magnetic field gradient applied at a series of equally-spaced angles around the tubes, a two-dimensional map of the distribution of proton concentration can be reconstructed (Lauterbur, 1973), using the principle now known generally as computed tomography.

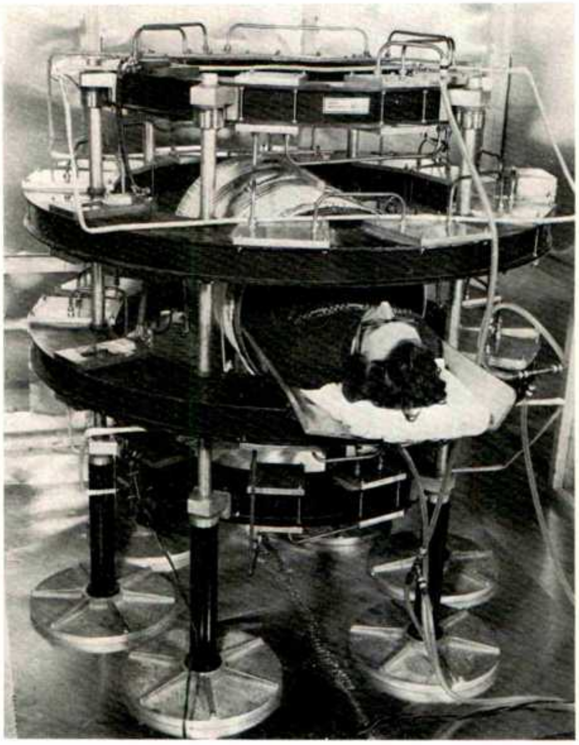


Fig. 15.

The Aberdeen whole-body NMR imaging machine (before completion). Dr. J. M. S. Hutchison is in the position of the patient. The machine is screened from radiofrequency interference by the surrounding metal room.

The NMR imaging programme in Aberdeen began in 1974 by producing an image of a whole mouse using this method (Hutchison *et al.*, 1974), which by displaying T_1 from point to point demonstrated liver of short T_1, brain of longer T_1 and tissue oedema of longest T_1.

*The Aberdeen NMR whole-body imaging machine**

Complete descriptions of the present machine and its electronic subsystems are given in Hutchison *et al.* (1980). It is based on a four-coil, air cored-electromagnet manufactured by the Oxford Instrument Company (Fig. 15). It produces a static magnetic field of 0.04 T and a consequent NMR frequency of

---

*The methods used are protected by patents held by the National Research Development Corporation, 66–74 Victoria Street, London SW1.

1.7 MHz for the hydrogen protons of body tissues. This field is applied in the PA direction of a supine patient.

The machine uses the NMR signals from hydrogen protons in water and in fat. It produces two kinds of image. The first uses proton density as the imaging parameter, and the second uses proton spin-lattice relaxation time (T_1). T_1 in wet tissues depends essentially on the relative proportions of free and bound water within the tissue under examination: tissues with more free water have longer relaxation times (Packer, 1977). T_1 values of normal and malignant animal and human tissues have been presented (Damadian *et al.*, 1973; Ling *et al.*, 1980; Mallard *et al.*, 1980) and their implications for *in vivo* clinical NMR imaging have been discussed.

The imaging principle employed is that of "selective excitation" (Mansfield *et al.*, 1976; Hutchison, 1976). The particular form used (Edelstein *et al.*, 1980) tolerates a much larger non-uniformity in magnetic field than the projection reconstruction method (Hutchison *et al.*, 1978; Sutherland and Hutchison, 1978) and also the effect of movement by the patient is less drastic. It uses a spectrally-shaped radiofrequency (RF) pulse in the presence of a field gradient to excite spins in a thin slice of the three-dimensional sample. In the simplest form of this technique, the field gradient is then turned through 90° to a direction parallel to the selected slice, and the spectrum or Fourier transform of the resulting free induction signal then represents the distribution of spins within the slice along the second gradient direction. So far there is no discrimination in the third orthogonal direction, and any image formed is a projection or shadowgraph in this direction.

In order to discriminate in the third direction and achieve true tomographic images, it is necessary to employ a field gradient in this direction together with some selective process. The most recent selective process which we use is called spin-warp imaging (Mallard *et al.*, 1981a; Edelstein *et al.*, 1980).

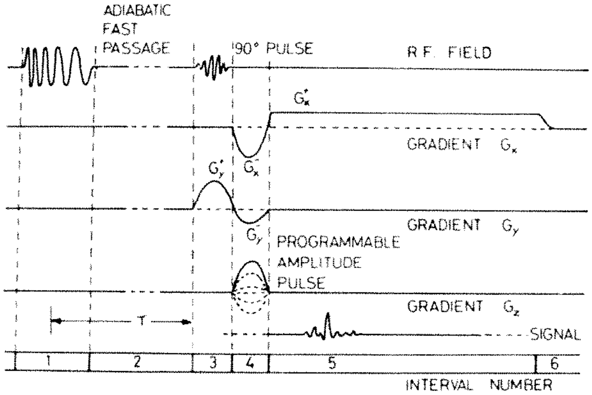


Fig. 16.

The RF and magnetic field gradient pulse sequence (Edelstein *et al.*, 1980; Mallard *et al.*, 1981a)

The pulse sequence used for the new imaging method is shown in Fig. 16. This refers to a set of co-ordinate axes with z vertical along the static field from posterior to anterior of a supine patient; y horizontal along the long axis of the patient from head to foot; and x horizontal laterally across the patient, from right to left.

Beginning at interval 3, a thin slab of spins transversely across the patient is selectively excited by the 90° RF pulse applied in the presence of a y magnetic field gradient. Following this excitation, a "readout" field gradient is applied in the x direction in interval 5 and the spectrum (more precisely, Fourier transform) of the free induction signal (sampled m times) is, in effect, a projection of the proton density in the slice onto the x-axis (as in Fig. 14, right). The frequency is directly related to the x-co-ordinate and the amplitude to the total spins in one of the m columns in the z direction (from back to front of the patient): there is no discrimination in the z-direction as yet.

The z-discrimination is obtained by taking n projections, all onto the same axis x. This would be a silly thing to do in isotope or X-ray tomographic imaging because the projection would be the same each time and thus projections have to be taken from different angles. What makes NMR different is the ability to use phase information in the signal. Each frequency component of the spectrum has phase information as well as amplitude: alternatively, it can be regarded as a complex number with both a real and an imaginary component.

Suppose then, a phase twist, or warp, is deliberately added to each column of spins, as shown in Fig. 17. Consider a long uniform column, as in column 1. When the contribution from each spin is added vectorially, the vector sum is quite small (there are about $1\frac{1}{2}$ full cycles of phase twist in this column). Column 2 has fewer spins in it but is divided into two separate portions. The gap could represent the air in the lungs, for example. The resultant vector sum is quite large with a phase angle slightly leftwards. Column 3 has the same structure as in column 2, but moved downwards a little in z. The vector sum has the same amplitude as in column 2 but is shifted in phase to be slightly rightwards. What has happened is that the phase twist maximizes the response to the spatial frequency related to the pitch of the phase twist.

This phase twist is introduced by adding a z field gradient pulse, G_z, after the selective excitation and before the readout, *i.e.* during interval 4 (Fig. 16). In each successive pulse sequence, G_z has the same shape but its amplitude changes by equal steps from zero to a maximum value, each one maximizing the response to a different spatial frequency in the z-direction. In practice, 64 of these pulse sequences are used from interval 3 onwards and a two dimensional Fourier transform of the m signals produces a $64 \times m$ image. They are called S_0 signals and contain mostly proton density information.

The above sequence is similar in principle to one proposed by Richard Ernst and colleagues (Kumar *et al.*, 1975; Ernst, 1978) who changed the time interval of G_z rather than the amplitude, as used here. The present method relaxes the stringent homogeneity of the static magnetic field required by Ernst's method.

Information on spin-lattice relaxation time (T_1) can be obtained by starting the sequence at interval 1. The spins are inverted and one waits during interval 2 for a time approximately equal to the average relaxation time in the sample (200 ms) before following with the sequence starting with interval 3. This initial inversion is done here by using an adiabatic fast passage for which an RF magnetic field in the rotating frame gives more than 90% inversion. Signals derived from the pulse sequence starting with interval 1 are called S_2 signals and contain information on both proton density and T_1 relaxation time.

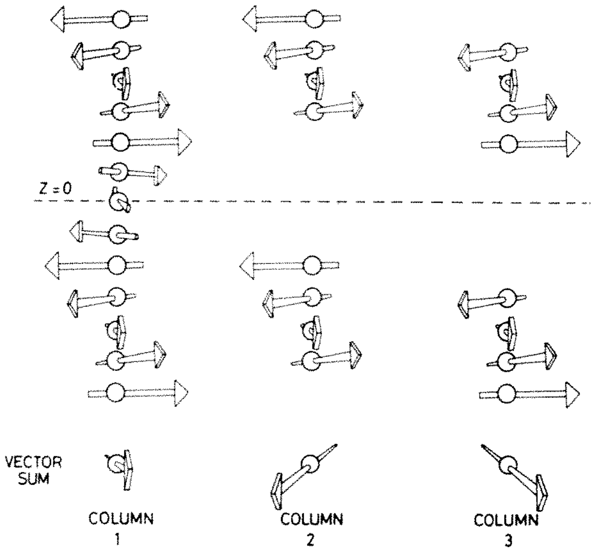


Fig. 17.

Pictorial representation of the phase twist introduced to a column of spins (Column 1) by applying a field gradient up the column. Columns 2 and 3 illustrate the phase change introduced into the vectorial sum of spins by changing the position of a gap in the column of spins.

Each pulse sequence takes one second. A 128-second scan collects data for both a proton density and a T_1 image. Such a scan consists of 64 signals of type S_0 and 64 signals of type S_2. One echo signal is collected each second. Initially, the S_0 data and the S_2 data are Fourier-transformed into two 64×64 element arrays. The T_1 value for each imaging element is calculated from the formula $T_1 = 200/\ln(2S_0/(S_0 - S_2))$. The 64×64 element S_0 and T_1 arrays are then interpolated into 256×256 arrays and displayed on a CONRAC CT-display* using 16 colour-coded levels, or a grey scale.

The tomographic sections have a Gaussian profile with thickness (equivalent rectangular width) 18.5 mm. Each imaging element is 7.5 mm wide ×7.5 mm high ×18.5 mm thick, comprising a volume of 1 cm^3. In each imaging element, the uncertainty in proton density for muscle tissue is about 2.5% and the uncertainty in T_1 is about 3.5% for T_1 close to 200 ms, with some worsening as T_1 departs from that optimum value.

Supporting programme of biological NMR measurements in vitro

The human body is extremely complex. When, in addition, we first attempt to image a new property such as proton magnetic resonance, there is bound to be difficulty in interpreting the results. To these difficulties, further confusion may be added if early NMR images are compared with other images derived from completely different tissue properties, *e.g.* X-ray absorption, radiopharmaceutical concentration, or ultrasound characteristic impedance. It has always been our intention, confirmed by the early animal images (Hutchison *et al.*, 1974), to attempt to image T_1 separately from proton concentration. With this in mind, we have carried out a biological back-up programme of T_1 measurements on normal and pathological tissues to ease the problem of image interpretation and to find pointers towards the most fruitful fields for the application of NMR imaging (Gordon 1975; Ling *et al.*, 1980; Mallard *et al.*, 1980).

Studies were made of a wide range of normal rabbit tissues at 24 MHz and 2.5 MHz. The values range from the lowest of 141 ms for liver to 463 ms for testis, with the body fluids, bile and blood serum being much higher at over 800 ms at 2.5 MHz, the frequency closest to our imaging frequency.

---

*Generously presented by Technicare Inc., Solon, USA.

For free water the relaxation time T_1 is about 3 s and it is believed that the very much reduced T_1 values for tissues are associated with the way in which the water is bound to proteins in the cells and the tightness of that binding. The closer the binding, the shorter the relaxation time.

For the soft tissues, there is a three-fold range of T_1 values which, together with the 3.5% uncertainty, offers good soft tissue discrimination. The water content of soft tissues ranges only from a minimum of 69% for skin through 79% for skeletal muscle, spleen and lung, to a maximum of 83% for grey brain tissue (72% for white brain tissue).

Many groups have measured the relaxation time of water protons in tumours. Results have indicated that malignant tissues generally have longer relaxation times than the equivalent normal tissues (Damadian *et al.*, 1973; Hollis *et al.*, 1973) although it is now recognized that there is a considerable overlap of values (Eggleston *et al.*, 1975; Koutcher *et al.*, 1978). *In-vitro* results obtained in this laboratory (Gordon 1975; Gordon *et al.*, 1978; Ling *et al.*, 1979) have been reviewed in Mallard *et al.* (1980) and were in accord with those of other workers. Very small scale studies suggested that perhaps human breast tumours and liver metastases might have an increased T_1 sufficiently above their surroundings for detection.

The effects on T_1 caused by biological processes such as inflammation, local immune reactions and invasion of neighbouring tissue by tumour were examined (Ling *et al.*, 1979). It was found that rat muscle immediately adjacent to implanted Yoshida sarcoma showed increased T_1 relaxation time, which gradually fell to the normal muscle value as one progressed further away from the tumour. Although this should have the effect of blurring the edge of a tumour and decreasing the resolution of the image, there may, perhaps, be a gain in that small tumours may appear (on T_1 images) to be larger than they are: this might help to detect them earlier.

It is important to realize that many clinical conditions other than malignancy may change the T_1 of body tissues. A condition which gives rise to a change in water content of a tissue, either intracellular or extracellular, *e.g.* oedema, should increase T_1 in the affected region. A considerable number of suggestions have been made to the speaker (see Mallard *et al.*, 1980) of potential diagnostic or investigative clinical uses of NMR imaging.

Safety aspects

The potential hazards of NMR imaging need to be investigated more precisely, although in the present generation of machines there seems to be little chance of serious effect upon the patient. A Working Party on the subject set up by the UK National Radiological Protection Board has reported recently (NRPB 1980).* The possible hazards include tissue heating by the radiofrequency fields and the effect of currents induced by the pulses of magnetic field gradient. The effect of the static magnetic field is believed to be less significant but should be kept below 2.5 T or 25000 Gauss (*ibid.*). The Aberdeen machine operates at 0.04 T.

The limit set upon the allowed radiofrequency heating effect has been based on not exceeding the basal metabolic rate, which is approximately 1 W/kg or 70 W total. The Aberdeen level is only up to 0.25 W to the whole body. Also, varying fields of 20 T/s are believed not to cause biological effects. In our machine the peak rate of change of field just reaches 3 T/s near the ends of the patient tube.

It is worth stressing that volunteers are quite unaware of the presence of any of the fields, or any subjective effects due to them.

Conditions which are advisable for human NMR imaging experiments during the very early stage of its use have been suggested (*ibid.*). Healthy volunteers should not be epileptics or have heart disease or, at the present state of knowledge, be pregnant. There should be a medical examination beforehand, a few days after and six months later, and during the exposure a person should be present with resuscitation equipment. For patients, the NMR image must be additional to all normal clinical procedures and a doctor should be present with resuscitation equipment. For both, records should be kept and pulse rate and reaction times observed during exposure. These recommendations will be reviewed after more experience has been gained.

This new imaging technique has the advantage of not using ionizing radiation, and it appears to be a safe, non-invasive procedure. A major investigation is underway in Aberdeen by Dr. Foster to attempt to discover and explore any short-term or long-term effects.

In-vivo *NMR images*

Results from a series of normal volunteers imaged in the machine described here have been reported by Edelstein *et al.* (1981). A considerable number of normal organs and structures can be imaged. I am grateful to Dr. Frank Smith, Consultant in Nuclear Medicine in Aberdeen, for help with these few cases collected from a clinical series which, at the time of

---

*Available from National Radiological Protection Board, Harwell, Didcot, Oxfordshire.

TABLE IV

SOME TYPICAL SPIN-LATTICE RELAXATION TIMES (MS) OF HUMAN TISSUES

Measured from *in-vivo* NMR images at 1.7 MHz			
Normal tissues			
Skeletal muscle	90–110	Fat	130–160
Liver	140–170	Pancreas	180–200
Bone	190–220	Cardiac muscle	240–260
Eye	240–260	Spleen	250–290
Cerebral cortex	250–300	Cerebellar cortex	250–300
Bile ducts	250–300	Spinal cord	290–300
Kidney	300–320		
Blood	350–420	Bile in gall bladder	300–700
CSF	800–1000	(depending on obstruction or not)	
		Urine	> 1000
Pathology			
Cirrhosis	180–300		
Liver tumours	300–450		
Lung carcinoma	350–400		
Renal carcinoma	400–450		

this lecture, exceeds 120 patients. Some other preliminary reports are now appearing (Smith *et al.*, 1981a; b; c; Mallard *et al.*, 1981a; b). The NMR images are colour coded in T_1 (or proton concentration) the code being displayed at the side of each image, the bottom (black, dark blue) being short T_1 and the top (white) having the value of T_1 printed adjacent.

Figure 18A shows an X-ray CT head section of a middle-aged man who was investigated following an epileptiform fit. A cystic glioma in the left parietal region was demonstrated. Figure 18B shows the equivalent NMR T_1 image. White matter is seen as two shades of yellow, grey matter as deeper yellow and red. The frontal air sinus is seen as black and the falx filled with blood as white-lilac. The cystic tumour mass is seen clearly (the X-CT image is displayed with left and right reversed), with a fluid level (probably caused by cellular debris) not seen on the X-ray image. The tumour itself is seen separately above the cyst.

Figure 19 shows an NMR T_1 abdominal cross-section of a 65-year-old man who complained of abdominal pain. Repeated ultrasound investigation was normal, as was a barium meal and follow through. The NMR T_1 section shows the aorta, spine, duodenum, normal right lobe of liver, tail of pancreas, and a high T_1 region suggesting a carcinoma of the head of the pancreas. On repeating the ultrasound scan, it suggested malignant nodes in the porta hepatis. Carcinoma pancreas was confirmed at laparotomy. Note that gas in the gut appears as black.

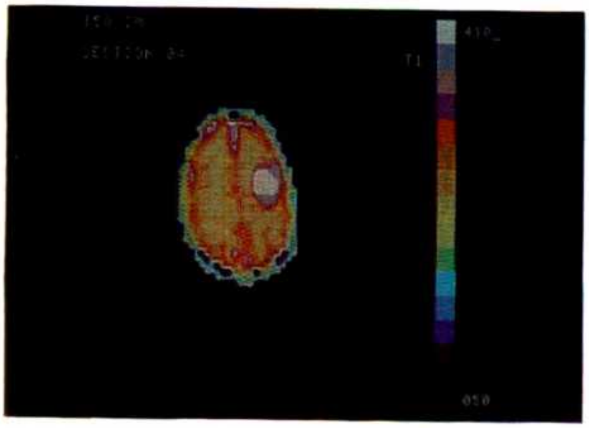
The pancreas is seen in only about 10% of cases but it is believed that we are not taking enough sections close enough to each other in this region. Pancreatitis has now been demonstrated in other patients where it is seen as a swollen gland of longer than normal T_1.

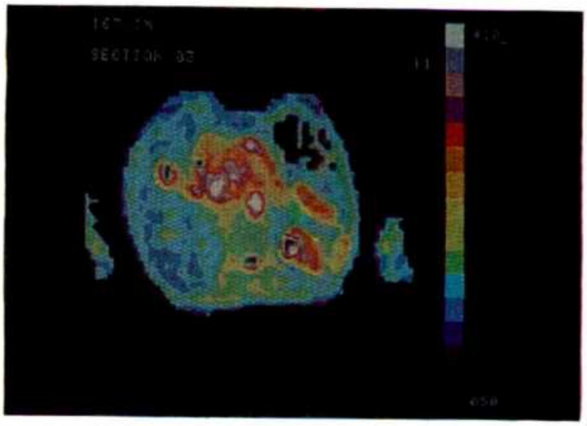
Figure 20A shows a NMR T_1 thoracic section of a 64-year-old man who presented with a vague abdominal pain. Ultrasound and radionuclide liver scans demonstrated intrahepatic tumour. A chest radiograph demonstrated a large pulmonary tumour which is seen here. In addition, the descending aorta, ascending aorta, superior vena cava and pulmonary artery are demonstrated. Figure 20B shows an abdominal section of the same patient, demonstrating large secondary deposits in the left lobe of the liver. The spleen, left kidney and spine are also seen.

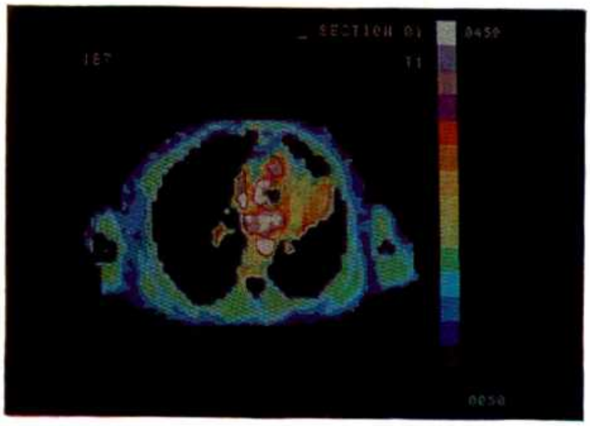
Figure 21A is an abdominal section of a $4\frac{1}{2}$ month pregnancy. The patient had a high alpha-feto-protein characteristic of an anencephalic fetus. This NMR section was taken immediately before termination. This is a proton concentration image which shows the pelvic bones well and abdominal fat. The uterus, fetus and amniotic fluid are imaged. Figure 21B shows the T_1 image of the same section. Whilst the extent of the amniotic fluid is seen more clearly, the fetus itself is seen less clearly. The uterine arteries are seen.

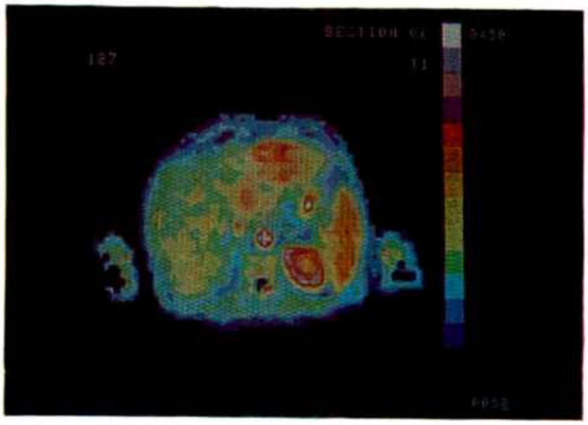
No untoward effects at all have been observed in the 140 people studied. The T_1 images seem to be particularly useful, but the proton concentration images are better at showing bone and fat.

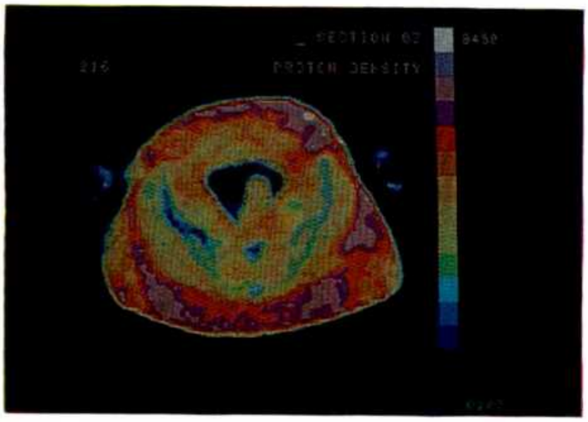
Table IV collects T_1 values determined from the clinical images. They agree well with those from the biological work referred to earlier. The soft tissues range from muscle at 100 ms, fat at 130 and liver at 140 ms, to kidney at 320 ms. This is a very big range which helps tissue discrimination. Measuring T_1 aids











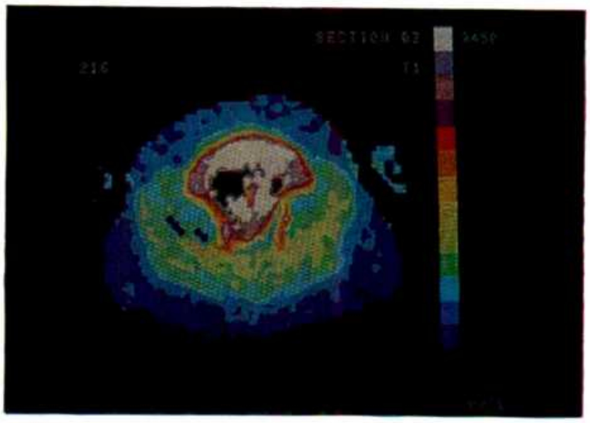


Fig. 18B	Fig. 19
Fig. 20A	Fig. 20B
Fig. 21A	Fig. 21B

Fig. 18. (B) The same section as (A) as demonstrated by T_1 NMR imaging.

Fig. 19. Abdominal section T_1 NMR image of carcinoma of head of pancreas.

Fig. 20. (A) Thoracic section T_1 NMR image showing large pulmonary tumour.
(B) Abdominal section T_1 NMR image of same patient showing large secondary malignant deposits in the left lobe of liver.

Fig. 21. (A) Abdominal section proton concentration NMR image of $4\frac{1}{2}$ month pregnancy (immediately before termination of anemophobic fetus).
(B) T_1 NMR image of same section.

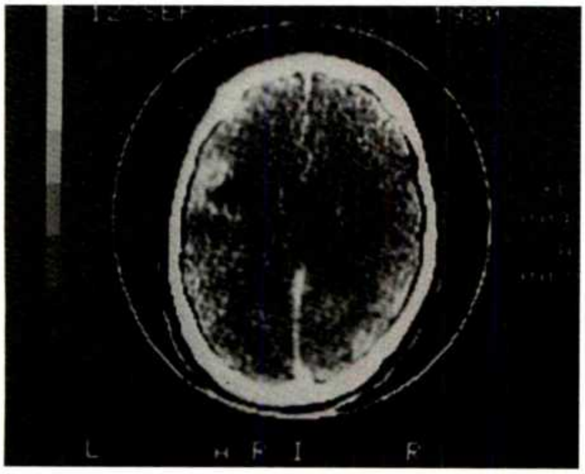


FIG. 18A.

(A) A cystic glioma in the left parietal region as demonstrated by X-ray CT imaging.

identification of tissues and fluids and this has proved a valuable clinical asset. Blood vessels are seen well because of the high T_1 value for blood. Bile and CSF is seen clearly too. Tumours are seen well because they have an increased T_1 above normal.

In general, the NMR images show both anatomical features and pathology. The method seems to present a combination of X-ray CT and nuclear medicine, because it shows some of the anatomy of X-ray CT with some of the physiology seen in the nuclear medicine image. It seems to have the advantage over nuclear medicine of having much more normal anatomy in an image which displays the pathology as well. Also the tumours are all seen as positive increases, and not holes or defects.

At present the spatial resolution is not so fine as X-ray CT. Our present images are produced by a machine resolution of 7.5 mm square, produced as 64×64 pixels. It is hoped to increase this to 128×128 pixels of data acquisition. At present the images are improved by displaying them as 256×256 even though the data acquisition is only 64×64. The thickness of the section displayed is 18 mm so that the pixel volume is about 1 cm^3.

The data for two images of each section are acquired in 128 seconds. It is hoped to improve this by at least four times. Perhaps dynamic heart studies will become possible. At present we discriminate between changes of T_1 of 3.5% and changes of proton concentration of 2.5%. Perhaps some of this T_1 discrimination can be traded off for further improvement in resolution.

All these images have been obtained by merely putting the patient into the machine, two minutes eight seconds for each pair of sections—one of T_1, one of proton concentration. There are no injections. The images portray the natural properties of the protons of the water, or fat, showing where they are and indicating whether or not they are tightly bound.

It is possible, indeed probable, that paramagnetic materials such as transition metal ions and oxygen will be used to alter the T_1 of some tissues and thereby alter the contrast on NMR images. Other teams have demonstrated that this may have clinical use for localizing tissue ischaemia (Doyle *et al.*, 1981). The years ahead will show whether the spin properties of phosphorus 31 and carbon 13 nuclei may ever prove capable of human *in-vivo* NMR investigation—even if not imaging—to add yet another dimension to NMR diagnosis.

Since this is the beginning of the clinical use of a new branch of imaging, I wonder if I dare suggest a name for them. We can all agree that we are talking about an NMR image. So if we say image in the French way as "im-ar-ge", so that it becomes en em ar im-arge, then we can drop a couple of syllables and and it becomes "en em arge" or "N-image". Whatever they are called, it looks as if magnetism in the form of NMR does offer medicine a new direction forward.

The title of this Memorial Lecture was "The Noes have it. Do they?" It was based upon the tradition in the House of Commons when a vote is taken. The result is declared in a loud voice "The Ayes have it" or "The Noes have it." By the Noes I mean the non-ionizing radiations and the non-conventional methods which are now in their infancy—so do the Noes have it? I think they might—they show great promise. It seems appropriate to end with a quotation from Tennyson's *In Memoriam*.

So many worlds, so much to do,
So little done, such things to be.

ACKNOWLEDGMENTS

I am deeply grateful to the University of Aberdeen, the Medical Research Council and the Cancer Research Campaign for their support for work described in this Lecture.

I have tried very hard to give full published references as acknowledgment of the work of my friends and colleagues, which I have collected together into this manuscript. If there have been any omissions, I apologize most sincerely. From amongst them all, I am especially grateful to Dr. K. V. Ettinger, Dr. D. J. Watmough, Dr. J. M. S. Hutchison and Dr. F. W. Smith, for their eager and willing help and support during its gestation. To my secretary, Miss I. Thomson, and to our graphics expert, Mr. R. Hutcheon, thank you for your excellent work in trying circumstances. To my wife and daughter, gratitude for the opportunity, the inspiration and the will.

REFERENCES

ATARI, N. A., ETTINGER, K. V. and FREMLIN, J. H., 1973. *Radiation Effects*, *17*, 45.

Bailey, H., 1936. Pocket transilluminoscope. *Lancet, i*, 902.

Cutler, M., 1929. Transillumination as an aid in the diagnosis of breast lesions. *Surgery in Gynaecology and Obstetrics, 48* (6), 721–729.

Damadian, R., Goldsmith, M. and Minkoff, L., 1977. NMR in cancer. Fonar image of the live human body. *Physiological Chemistry and Physics, 9*, 97–100.

Damadian, R., Zaner, K., Hor, D., Dimaio, T., Minkoff, L. and Goldsmith, M., 1973. Nuclear magnetic resonance as a new tool in cancer research: tumours by NMR. *Annals of the New York Academy of Sciences, 222*, 1048.

Doyle, F. H., Gore, J. C. and Pennock, J. M., 1981. Relaxation rate enhancement—observed *in-vivo* by NMR imaging. In *Proceedings of the 1st NMR Imaging Symposium*, Vanderbilt University, Nashville, October 1980. *Journal of Computer Assisted Tomography*, (in press).

Edelstein, W. A., Hutchison, J. M. S., Johnson, G. and Redpath, T. W., 1980. Spin Warp NMR imaging and applications to human whole-body imaging. *Physics in Medicine and Biology, 25*, 751–756.

Edelstein, W. A., Hutchison, J. M. S., Smith, F. W., Mallard, J., Johnson, G. and Redpath, T. W., 1981. Human whole-body NMR tomographic imaging: normal sections. *British Journal of Radiology, 54*, 149–151.

Eggleston, J. C., Saryan, L. A. and Hollis, D. P., 1975. Nuclear Magnetic Resonance investigations of human neoplastic and abnormal non-neoplastic tissues. *Cancer Research, 35*, 1326–1332.

Ernst, R. R., 1978. Gyromagnetic resonance Fourier transform Zeugmatography. *US Patent* 4070611.

Ettinger, K. V., Mallard, J. R., Anunuso, C. I., Del Vigna Filho, E., Regan, C. and Srirath, S., 1980. Applications of lyoluminescence. *Nuclear Instruments and Methods, 175*, 136–138.

Ettinger, K. V., Mallard, J. R., Srirath, S. and Takavar, A., 1977. Lyoluminescence dosimetry with some saccharides. *Physics in Medicine and Biology, 22*, 3, 481–489.

Foster, M. A. and Hutchison, J. M. S., 1980. Imaging by nuclear magnetic resonance. *Aberdeen Postgraduate Medical Bulletin, 14*, 2, 7.

Gordon, R. E., 1975. Proton NMR relaxation time measurements in some biological tissues. Ph.D. Thesis, University of Aberdeen.

Gordon, R. E., Mallard, J. R. and Philip, J. F., 1978. Chapter 16 in *Nuclear Magnetic Resonance Effect in Cancer*. Ed. by R. Damadian (Pacific Publishing Co., Portland, Oregon).

Hardy, J. D., Hammel, H. T. and Murgatroyd, D., 1956. Spectral transmittance and reflectance of excised human skin. *Journal of Applied Physiology, 9*, 257–264.

Hardy, J. D. and Muschenheim, C., 1934. The radiation of heat from the human body. IV. The emission, reflection and transmission of infra-red radiation by the skin. *Journal of Clinical Investigation, 13*, 817–831.

Hinshaw, W. S., 1976. Image formation by nuclear magnetic resonance: the sensitive point method. *Journal of Applied Physics, 47*, 3709–3721.

Holland, G. N., Hawkes, R. D. and Moore, W. S., 1980. NMR tomography of the brain. *Journal of Computer Assisted Tomography, 4*, 429–433.

Hollis, D. P., Economou, J. S., Parks, L. C., Eggleston, J. C., Saryan, L. A. and Czeisler, J. L., 1973. Nuclear magnetic resonance studies of several experimental and human malignant tumors. *Cancer Research, 33*, 2156–2160.

Hoult, D. I., 1979. Rotating frame zeugmatography. *Journal of Magnetic Resonance, 33*, 183–197.

Hussey, G., Macdonald, A. F., Nichols, D. and Watmough, D. J., 1981. Diaphanography—a comparison with mammography and thermography. *Proceedings of Symposium Mammographicum 80*, London 1980. *British Journal of Radiology, 54*, 163.

Hutchison, J. M. S., 1976. Imaging by nuclear magnetic resonance. *Proceedings of the 7th L. H. Gray Conference on Medical Images, Leeds*. Ed. by G. A. Hay, (Institute of Physics, Bristol/Wiley), pp. 135–141.

Hutchison, J. M. S., Edelstein, W. A. and Johnson, G., 1980. A whole-body NMR imaging machine. *Journal of Physics E: Scientific Instruments, 13*, 947–955.

Hutchison, J. M. S., Mallard, J. R. and Goll, C. C., 1974. In-vivo imaging of body structures using proton resonance. *Proceedings of the 18th Ampere Congress*, Nottingham, Ed. by P. S. Allen, E. R. Andrew and C. A. Bates, (University of Nottingham), pp. 283–284.

Hutchison, J. M. S., Sutherland, R. J. and Mallard, J. R., 1978. NMR imaging: image recovery under magnetic fields with large non-uniformities. *Journal of Physics E: Scientific Instruments, 11*, 217–221.

Hynynen, K., Watmough, D. J. and Mallard, J. R., 1981a. Design of ultrasound transducers for local hyperthermia. *Ultrasound in Medicine and Biology* (in press).

1981b. The effects of some physical factors on the production of hyperthermia by ultrasound in neoplastic tissues. *Radiation & Environmental Biophysics* (in press).

Kikuchi, Y., Uchida, R., Tanaka, K. and Wagai, T., 1957. Early diagnosis through ultrasonics. *Journal of the Acoustical Society of America, 29*, 824–833.

Koutcher, J. A., Goldsmith, M. and Damadian, R., 1978. NMR in cancer. X. A malignancy index to discriminate normal and cancerous tissue. *Cancer, 41*, 174–182.

Kumar, A., Welti, D. and Ernst, R. R., 1975. NMR Fourier Zeugmatography. *Journal of Magnetic Resonance, 18*, 68–83.

Lauterbur, P., 1973. Image formation by induced local interactions, examples employing nuclear magnetic resonance. *Nature, 242*, 190.

Lele, P. P., 1975. Hyperthermia by Ultrasound. *Proceedings of the International Symposium on Therapy by Hyperthermia & Radiation*, Washington. April 1975 (American College of Radiologists).

1979. A strategy for localized chemotherapy of tumours using ultrasonic hyperthermia. *Ultrasound in Medicine and Biology, 5*, 95–97.

Ling, C. R., Foster, M. A. and Hutchison, J. M. S., 1980. Comparison of NMR water proton T_1 relaxation times of rabbit tissues at 24 MHz and 2.5 MHz. *Physics in Medicine & Biology, 25*, 748–751.

Ling, C. R., Foster, M. A. and Mallard, J. R., 1979. Changes in NMR relaxation times of adjacent muscle after implantation of malignant and normal tissue. *British Journal of Cancer, 40*, 898–902.

Mallard, J. R., Hutchison, J. M. S., Edelstein, W. A., Ling, C. R., Foster, M. A. and Johnson, G., 1980. In-vivo NMR imaging in medicine: the Aberdeen approach, both physical and biological. *Philosophical Transactions of the Royal Society of London, B, 289*, 519–533.

Mallard, J. R., Hutchison, J. M. S., Foster, M. A., Edelstein, W. A., Ling, C. R., Smith, F. W., Reid, A., Selbie, R., Johnson, G. and Redpath, T. W., 1981a. Medical imaging by Nuclear Magnetic Resonance—a review of the Aberdeen Physical and Biological Programme. *IAEA International Symposium on Medical Radionuclide Imaging*, Heidelberg, Germany, September 1980. (IAEA-SM-247/201) (International Atomic Energy Agency, Vienna).

Mallard, J. R., Smith, F. W. and Hutchison, J. M. S., 1981b. *Medical Tribune Circulation Today, 2*, (26), 27.

Mansfield, P., Maudsley, A. A. and Baines, T., 1976. Fast scan proton density imaging by NMR. *Journal of Physics E: Scientific Instruments, 9*, 271–8.

Mansfield, P. and Pykett, I. L., 1978. Biological and medical imaging by NMR. *Journal of Magnetic Resonance, 29*, 69–83.

NCRP Report 66, 1980. Mammography. (National Council on Radiation Protection and Measurements, Washington, DC).

NRPB, 1980. Outline of advice on exposure to nuclear magnetic resonance clinical imaging. NMR 2/80/3.

(National Radiation Protection Board, Harwell) (in press).

Ohlsson, B., Gundersen, J. and Nilsson, D. M., 1977. Diafanograft—en ny metod for utdersokning av brostet. (Diaphanography—a new method for investigation of the breast). *Lakarsallskapets Riksstamma Sammanfattningar*, (Abstracts of Swedish Medical Society annual meeting, Stockholm 1977), p. 364

Packer, K. J., 1977. The dynamics of water in heterogeneous systems. *Philosophical Transactions of the Royal Society of London B, 278*, 59–87.

Short, J. G. and Turner, P. F., 1980. Physical hyperthermia and cancer therapy. *Proceedings of the IEEE, 68*, 133–142.

Smith, F. W., Hutchison, J. M. S., Johnson, G., Mallard, J. R., Reid, A., Redpath, T. W. and Selbie, R. D., 1981a. Clinical application of nuclear magnetic resonance. *Lancet*. January 10, 78–79.

Smith, F. W., Hutchison, J. M. S., Mallard, J. R., Johnson, G. Redpath, T. W., Selbie, R. D., Reid, A. and Smith, C. C., 1981b. Oesophageal carcinoma demonstrated by wholebody nuclear magnetic resonance imaging. *British Medical Journal, 282*, 510–512.

Smith, F. W., Hutchison, J. M. S., Mallard, J. R., Reid, A., Johnson, G., Redpath, T. W. and Selbie, R. D., 1981c. Renal cyst or tumour—differentiation by wholebody nuclear magnetic resonance imaging. *Diagnostic Imaging, 50*, 61–65.

Strax, P., 1980. An overview of breast cancer; defining the problem. *Medical Progress and Technology, 7*, 2–3, 131–137.

Sutherland, R. J. and Hutchison, J. M. S., 1978. Three-dimensional NMR imaging using selective excitation. *Journal of Physics E: Scientific Instruments, 11*, 79–83.

Thompson, J. S. and Thompson, H. G., 1920. *Silvanus Phillips Thompson: His Life and Letters* (Unwin, London).

Watmough, D. J., 1981. Personal communication.

1981. Tele-diaphanography: a new approach to the detection of breast disease (in preparation).

Watmough, D. J., Pratt, B., Wong, S. Y. and Mallard, J. R., 1980. A study of the effects of ultrasound on HeLa cells and other biological materials by means of optical microscopy with a view in the longer term to treating malignant tissues. *Proceedings of the First Spring School on Acousto-Optics and Applications.* May 1980 (Gdansk, Poland).

Wilson, A. K., 1936. Transillumination of breast. *West Virginia Medical Journal*, pp. 32–245.

Wong, Y. S. and Watmough, D. J., 1981. Haemolysis of red blood cells in vitro and in vivo induced by ultrasound at 0.75 MHz and at therapeutic intensity levels. *Proceedings of Symposium of Ultrasound in Biology and Medicine*, Reinhardsbrunn, G.D.R. November 1980. (in press).

Zhuravlev, A. I., 1974. Spontaneous ultraweak metabolic luminescence of blood plasma and serum in the visible region. *Transactions of the Moscow Society of Naturalists, 50*, 9.

Book reviews

A Practical Introduction to Cranial CT. By A. R. Valentine, P. Pullicino and E. Bannan, pp. 149, 1981 (Heinemann, London), £8·00.
ISBN 0–433–336021

In the foreword to this book, Professor G. du Boulay states, "Everyone . . . needs what used to be known as a primer, on the subject of CT". This statement is completely true and within these limits—this is an excellent primer. The problem is that those asked to review primers in any subject have usually passed the stage of needing a primer. There is, therefore, a temptation to say "yes, that is true, but not always". or "why didn't the authors mention the limitations?" and yet again, "how about this or that technique?"

Such thoughts must be resisted in reading this book. There is a clear explanation of the technical aspects, and of certain practical aspects of CT cerebral scanning. A section on anatomy is clear and useful. A quick glance at Fig. 3·9(a) suggests motor tracts in both frontal poles—but it is presumed that the key applies only to Fig. 3·9(c). A very useful chapter gives advice on how to report a scan and makes the very cogent point that not all areas of low attenuation with atrophy are due to infarction.

The rest of the book is concerned with an analysis of intracranial lesions by their CT characteristics (*e.g.* low or high attenuation, mass effect, enhancement etc.). These chapters are clear, well illustrated and easily understood. The more advanced student will not find much concerning the limitations of CT in various situations, except in pontine lesions. The need for alternative techniques is not acknowledged. For example, nearly all aneurysms will require angiography and the great majority of berry aneurysms are very difficult and time-consuming to find on CT. Metrizamide cisternography is mentioned in the opening chapters – but not in relation to pituitary tumours or CP angle tumours.

These are some minor criticisms which centre around the difficulties of a primer. This is a good little book, providing potted didactic information on cranial CT. At £8 it is well within the financial range of any radiological trainee, and will satisfy a great need for those who will later control a general purpose CT scanner and have to perform cranial CT isolated from a Department of Neurosciences.

A. S. Bligh.

Manuel de Techniques Radiographiques du Crâne. By G. Korach and J. Vignaud. 2nd edit., pp. 144, 1980 (Masson, Paris), price not known.
ISBN 2–225–66572–9

This publication can only be highly recommended for those interested in radiography of the skull.

The initial chapters present in a concise manner the factors which influence radiographic quality with special reference to the skull. The theory of special techniques such as stereoradiography and tomography is dealt with simply, aided by excellent diagrams. The following chapters deal with technique and are quite superb giving precise patient positioning instructions accompanied by photographs, the resultant radiographs and anatomical line diagrams. The reproduction of the radiographs is excellent.

Therefore, this book is not only an aid to positioning but also to interpretation and therefore is of value both to the radiographer and the trainee radiologist.

J. F. Ellis

1981, *British Journal of Radiology*, *54*, 850–855

Rapid biomedical imaging by NMR

By R. J. Ordidge, P. Mansfield
Department of Physics, University of Nottingham
and R. E. Coupland
Department of Human Morphology, Queen's Medical Centre, University of Nottingham

(*Received July 1981*)

Abstract

The first biomedical images to be produced by the new high-speed echo-planar imaging technique are presented. Clear anatomical detail is revealed in both human and animal studies performed *in vivo*. The potential for imaging moving objects and flow is briefly discussed.

The first nuclear magnetic resonance (NMR) images to demonstrate clearly resolved human anatomical detail *in vivo* were performed by a line-scanning technique (Mansfield *et al.*, 1976; Mansfield and Maudsley, 1977). Since then we, as well as several other groups, have produced NMR images of various parts of the human anatomy including abdominal, thoracic and head scans (Bangert *et al.*, 1981; Damadian *et al.*, 1977; Edelstein *et al.*, 1981; Mansfield *et al.*, 1978; Holland *et al.*, 1980). All NMR imaging techniques measure the spatial distribution of mobile protons contained in the water, fat or oil distributed within the various tissues and organs of the body. The images referred to have been produced by an assortment of techniques and produced in times varying from several hours down to several minutes. Some of the improvement in imaging time can be ascribed to natural development of the subject, the more recent images being refinements and developments of earlier imaging schemes. A full description and discussion of the various techniques is given by Mansfield and Morris (1981). Imaging schemes fall into three main categories; point scanning, line scanning and planar imaging. The classification relates to the data collection mode and degree of data channel multiplexing. For equal resolution and signal/noise ratio of the image, point scanning is the slowest imaging method, the others being correspondingly faster.

It seems clear from a physiological point of view that fast imaging is to be preferred, especially when considering involuntary bodily movements. We may classify these movements broadly speaking on three time scales: breathing motion on a scale of around 20 s, gut motion on a scale of around 5 s and cardiac motion on a scale of around 0.8 s. For heads and limbs which may be clamped, the time regimes quoted are not important, though it is still desirable from the point of view of patient management to perform the imaging as speedily as possible.

The planar imaging methods referred to above rely either on a filtered back projection technique, which requires typically 128 separate spin density profiles or projections of the object before image reconstruction can commence, or on a two-dimensional Fourier transformation of transient data to produce the spin density distribution. Again, as with the projection method, the equivalent of 128 separate experiments must be performed and all the data gathered before computation of the image can proceed. Thus although both these methods are efficient in the sense that all spins within a predefined plane are simultaneously observed in each experimental "look", a certain pre-requisite number of looks is mandatory before one can start the image formation algorithm. For a final picture array of m^2 pixels, this minimum number of looks is approximately m.

When a spin system is perturbed from its normal equilibrium polarization state of alignment in the external static magnetic field, it requires a time of the order of T_1, the spin-lattice relaxation time, to re-equilibrate. In normal tissue T_1 varies over a range of around 100 ms to 600 ms depending on tissue type. For example, in liver, $T_1 \simeq 500$ ms. Using this value as an average for the body we see from the above discussion that we cannot expect to obtain an image in less than about 60 s by any of the above planar imaging methods.

These considerations have led us to seek new and faster imaging methods which do not sacrifice resolution or signal/noise in the final image. A method which achieves these aims was devised several years ago (Mansfield, 1977; Mansfield and Pykett, 1978) and is now referred to as echo-planar imaging. However, it is only recently that we have been able to translate the technique into a 1/4th human scale working system. In this paper, we wish to briefly

---

Reprint requests and correspondence: Professor P. Mansfield, Department of Physics, University of Nottingham, Nottingham NG7 2RO.

describe the echo-planar imaging method and present the first biomedical NMR images obtained by this new technique.

METHOD

The basic principle of echo-planar imaging has already been given by Mansfield (1977) (see also Mansfield *et al.* (1980)). Full description of the apparatus and pulse sequences used in the experiments described will be presented elsewhere. In this paper, therefore, we shall give only a brief outline of the echo-planar imaging method together with the experimental conditions used to obtain the results.

To explain and clarify the method we refer to Fig. 1. Consider an extended object containing mobile protons which is placed in a static polarizing field B_0. Localized spin polarization will reflect the spatial variations of water content, etc. throughout the specimen. If a magnetic gradient G_z is applied to the specimen together with a selective RF pulse, a thin slice of magnetization, thickness Δz, may be selectively perturbed from its equilibrium alignment. The transverse response or free induction decay (FID) of this slice is observed in a periodically switched gradient $\pm G_y$. If the FID is sampled and Fourier-transformed, we obtain the discrete spin projection edge profile as a function of ω_y which corresponds to spin density projections of successive shaded strips along the x-axis. We wish to obtain the spin density side profiles. These may be obtained by applying an additional steady broadening gradient G_x during the signal sampling period. This procedure turns the edge profiles into the broadened profiles which are now functions of both x and y. The broadening gradient effectively rotates the spin distribution, thus allowing a view of the total spin distribution between the rows. The broadened profiles contain all the information necessary to produce a complete image in a one-shot experiment which in the present case takes 41.0 ms. It should be emphasized that the high speed is not achieved at the expense of image resolution. Naturally, the signal/noise ratio of single shot images may be improved by $\sqrt{N}$ by signal averages over N one-shot experiments. In the present version of the experiment, a delay τ between shots is included, thus increasing the total experimental time to tens of seconds. Intrinsic motion in the object over this time scale thus produces a blurring of the image.

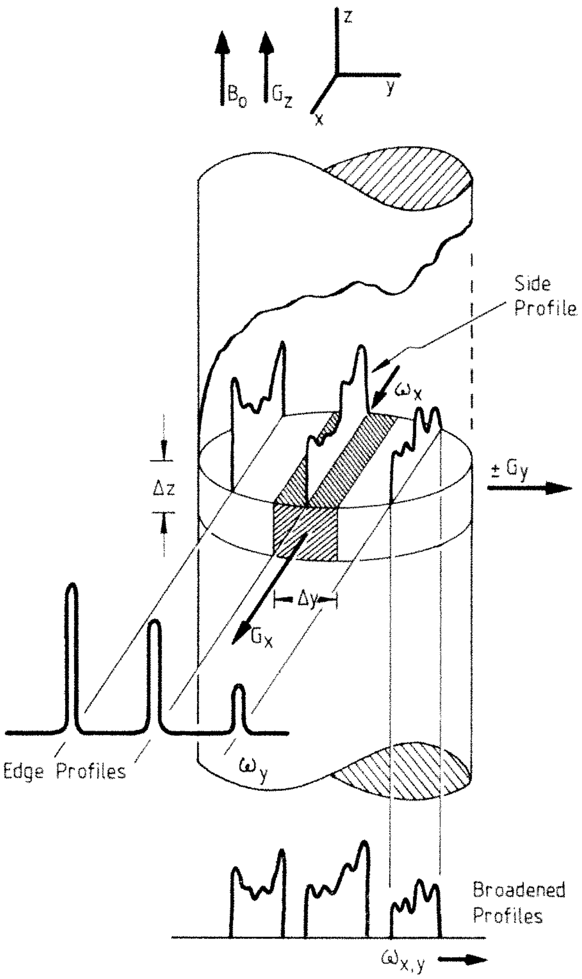


FIG. 1.

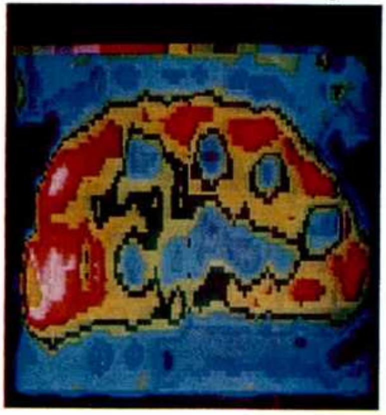
Sketch illustrating the various projections of spin density profiles in a slice of material isolated by selective excitation and subjected to switched gradients in the echo-planar imaging method. The side profiles indicated are not directly viewable but may be observed in combined switched y and steady x gradients to yield the broadened profiles. Also sketched are the edge profiles observable in G_y only.

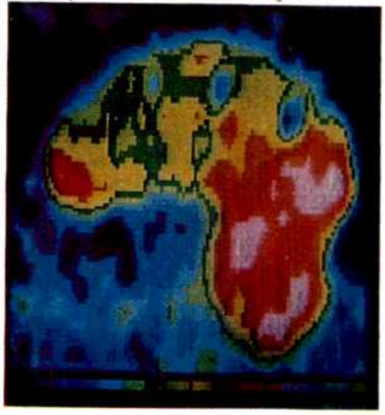
Data handling

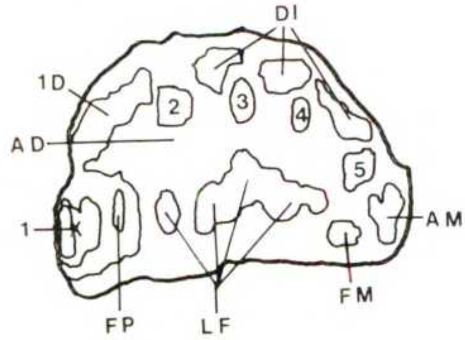
The switched gradient G_y produces a FID comprising a series of spin echoes. Odd and even echoes are always formed in negative and positive gradients respectively. It is therefore necessary to edit the FID, transforming the odd and even echo responses separately. The frequency domain profiles may then be reordered and added together to give a single picture. The editing process and data reordering are done under computer control.

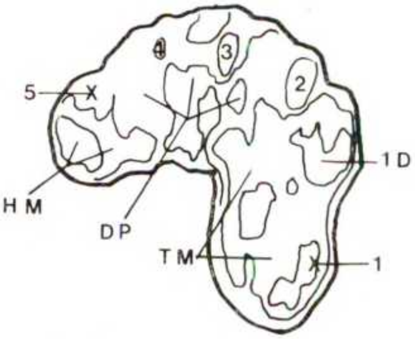
Apparatus

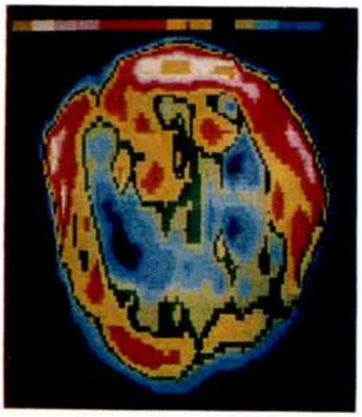
Full details of the apparatus will be described elsewhere. The main features are the use of focused selection of the initial slice (Hoult, 1977; Sutherland and Hutchison, 1978) and the switched field gradients. The gradient details are as follows. The

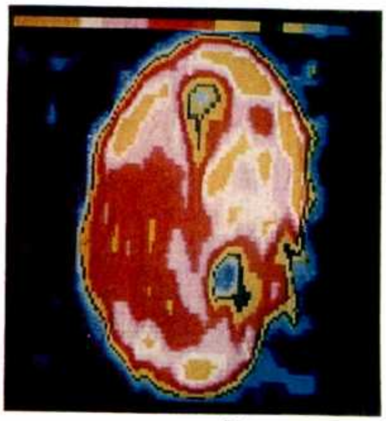


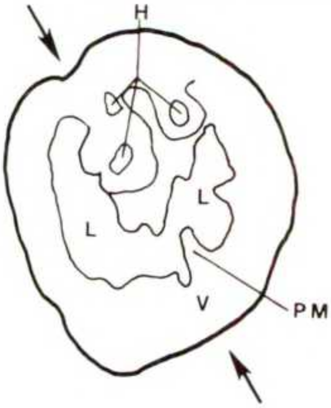


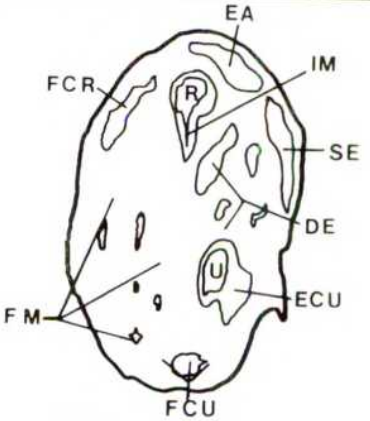












3A	2A
3B	2B
5A	4A
5B	4B

(*opposite*) FIG. 2A.

NMR echo-planar cross-section through the right hand at the level just proximal to the heads of the 2nd–4th metacarpals. Imaging time was 35 s, comprising 64 separate shots with delay between shots $\tau = 0.5$ s. Dark blue corresponds to low image intensity.

FIG. 2B.

Line tracing of Fig. 2A. 1–5 shafts of metacarpal bones. TM = thenar eminence; HM = muscle of the hypothenar eminence; DP = deep palmar tissues; 1D = first dorsal interosseous muscle.

FIG. 3A.

NMR echo-planar cross-sectional image through the junctions of the proximal $\frac{1}{3}$ and distal $\frac{2}{3}$ of the left hand palm. See Fig. 3B and text for structural and other details. Colour scale as for Fig. 2A.

FIG. 3B.

Line tracing of Fig. 3A. 1–5 shafts of metacarpals. 1D, first dorsal interosseous muscle; DI, other dorsal interossei; LF, long flexor tendons; FP, flexor pollicis longus tendon within the thenar muscles; FM, flexor digiti minimi; AM, abductor digiti minimi; AD, adductor pollicis.

FIG. 4A.

Cross-sectional echo-planar image through left forearm about 5 cm proximal to the head of the ulna. See Fig. 4B for structural details. Experimental details and colour scale as for Fig. 3A.

FIG. 4B.

Line tracing of Fig. 4A. R, shaft of radius; U, shaft of ulna; IM, interosseous membrane; ECU, exterior carpi ulnaris; FCU, flexor carpi ulnaris; FCR, flexor carpi radialis; EA, exterior and abductor muscles of thumb; SE, superficial extensor muscles and tendons; DE, deep extensor muscles; FM, long flexor muscles of digits, also shows tendon regions (yellow).

FIG. 5A.

Cross-sectional echo-planar image of the thorax of a rabbit at the level through the heart. The anterior aspect is to the top left. All experimental and display details as for Fig. 3A. See Fig. 5B for structural details.

FIG. 5B.

Line tracing of Fig. 5A. The upper arrow denotes the midline anterior aspect. H, chambers of the heart, L, lung fields, PM, posterior mediastinum.

selection gradient $G_z = 0.58$ G cm^{-1} with a rise time of 60 μs and a reversal time of ~ 90 μs. The peak RF power used was 5 W and the pulse length 3.7ms. The switched gradient $G_y = 0.65$ G cm^{-1} with a rise time of 26 μs and a reversal time of 52 μs. The number of cycles used is 32 and the total data collection time is 40.96 ms. In this time 2048 sample points are taken and Fourier-transformed using a real point transform only to yield 1024 frequency domain points. This gives a 32×32 picture matrix. All images have been linearly interpolated to 128×128 arrays. The broadening gradient $G_x = 0.02$ G cm^{-1} with a rise and fall time of 4.0 μs.

A trapezoidal coil design (Bangert and Mansfield, 1981) is used to produce G_x and G_y. A Maxwell pair is used to produce G_z. Particular attention must be paid to spatial linearity of the gradient coils. It is also important to have the positive and negative excursions of G_y properly balanced. Excessive static field inhomogeneity must also be shimmed out. Typical inhomogeneity over a 10 cm diameter disc of 8 mm thickness is 4×10^{-6}. The transmitter and receiver coils are saddle design (Mansfield and Morris, 1981) allowing specimen access along the B_0 axis.

RESULTS

A number of live biological specimens have been examined by echo-planar imaging. In all cases, the original image matrix comprises 1024 points which is interpolated to yield a 128×128 picture. All images are averaged for the stated times and number of shots. Each complete one-shot image is obtained in 45.91 ms including the initial focused selection procedure. Images of water phantoms and object/image comparisons give good results and will be discussed elsewhere. Slice thickness in all images is 8 mm and the proton resonance frequency is 4.0 MHz, corresponding to a static magnetic field of 940 G.

Human study

A number of NMR images have been taken of live human hands and arms. All data are presented in a 16-level colour scale to enhance image contrast. Dark blue corresponds to low signal intensity.

Figure 2A shows an NMR cross-sectional image through the right hand (R.J.O.) just proximal to the heads of the 2nd and 4th metacarpals and passing through the heads of the 1st and 5th metacarpals. This is an average of 64 shots taking an equivalent imaging time of 35 s. Figure 2B is a line tracing from 2A labelling the clear morphological detail. The thumb was held in a position of palmar abduction and the 1st metacarpal (labelled 1) has a similar signal intensity to the muscles of the thenar eminence (TM). Shafts of other metacarpal bones are indicated 2–4. Other features include muscles of the hypothenar eminence (HM) and the 1st dorsal interosseous muscle (1D). The deep palmar tissues (DP) include flexor tendons, small muscles of the palm, nerves and vessels.

Figure 3A shows an NMR cross-section through the junction at the proximal $\frac{1}{3}$ and distal $\frac{2}{3}$ of the left hand palm of P.G.M. (see Acknowledgments). The equivalent imaging time was 69 s corresponding to an average over 128 shots. The considerable detail evident in this image is labelled in Fig. 3B. Shafts of the metacarpals are indicated 1–5. Note the different signal intensity produced by the 1st metacarpal which reflects its different structure. The 1st dorsal interosseous muscle (1D) and the dorsal interossei (DI) show clearly at the intermediate signal level (red). The long flexor tendons (LF) and flexor pollicis longus tendon show as low signal zones, the latter surrounded by muscles of the thenar eminence. Other distinguishable regions include the flexor digiti minimi (FM), the abductor digiti minimi (AM) and the adductor pollici (AD). Deep palmar fascia, vessels and nerves and palmar interossei occupy the space between the long flexor tendons and shafts of the metacarpals.

Figure 4A is an NMR cross-section through the left forearm (P.G.M.) about 4 cm proximal to the head of the ulna. Experimental details were the same as for Fig. 3. Again, a number of clear anatomical details are evident as indicated in Fig. 4B. The shafts of the radius (R) and ulna (U) show as regions of low signal intensity. The interosseous membrane (IM) attached to the radius shows as level 7 (dark yellow) as do parts of the extensor carpi ulnaris (ECU). As expected, the soft tissue and muscle regions show as intense signal zones, for example the flexor carpi ulnaris (FCU), the flexor carpi radialis (FCR), the long and short extensor and long abductor muscle of the thumb (EA), the superficial extensor muscles and tendons (SE). The long flexor muscles of the digits (FM) do show slight differentiation within the red band, the fibrous tendon regions being of lower intensity (yellow).

Animal studies

Figure 5A shows an echo-planar cross-sectional image through the thorax of a live rabbit. The experimental details were as for Fig. 3. Clear delineation of the chest wall and interior is indicated. Morphological details are summarized in Fig. 5B. The arrows indicate the mid-line. The anterior aspect lies to the top left. The left side is to the right of the arrows. Features identifiable include chambers of the heart (H), lung fields (L) and posterior mediastinum (PM) which includes aorta and oesophagus. The vertebral column is situated at V.

CONCLUSIONS

These first biomedical images clearly demonstrate the potential for high-speed echo-planar imaging. However, the results also indicate that at present there are a number of limitations both in technique and equipment. Single shot images, not shown, typically give signal/noise ratios of around 2:1 and suggest that much-improved receiver electronics are required for full realization of the single shot or "instant" picture capability of the technique. However, theoretical results presented elsewhere (Mansfield and Morris, 1981) show that for optimum coil geometries and experimentally achievable receiver noise figures, the apparatus will scale to whole body size giving a 64×64 array with a single shot signal/noise ratio of about 6–7: 1 for a 10 mm slice. Such images could of course be averaged to improve signal/noise. For example, a signal/noise ratio of 16:1 could be produced in six shots taking about three seconds. However, it may be that in certain circumstances the single shot picture quality will be acceptable.

In the present images, there is evidence of unequal spatial resolution across and down an image. Steps are being taken to rectify this. The rapidly switched field gradient used (250 T $m^{-1}s^{-1}$) produced no sensation in the arm images, nor did it cause any observable effect in the rabbit. The mean RF power delivered at the probe head was 20 mW (5 W peak), only a small fraction of which is absorbed by the specimen.

With resolution and signal/noise improvements, this imaging technique has a number of important advantages over other slower techniques. There is for example, the possibility of imaging moving objects. This could be of importance in NMR cardiography, blood flow and internal motional studies. Even in cases where involuntary motion is not a problem, as in the head and limbs, a fast imaging technique could be valuable from the viewpoint of the comfort and management of the patient.

ACKNOWLEDGMENTS

We wish to thank Dr. P. G. Morris and Mr. R. Rzedzian for their help in some of the phases of this work. We are also grateful to the Medical Research Council and the Department of Health and Social Security for project grants to support this work. On of us (R.J.O.) wishes to thank the Science Research Council for a postgraduate studentship.

REFERENCES

Bangert, V. and Mansfield, P., 1981. Magnetic field gradient coils for NMR imaging. *Journal of Physics E* (in press).

Bangert, V., Mansfield, P. and Coupland, R. E., 1981. Whole-body tomographic imaging by NMR. *British Journal of Radiology*, *54*, 152–154.

Damadian, R., Goldsmith, M. and Minkoff, L., 1977. NMR in cancer: XVI. Fonar image of the live human body. *Physiological Chemistry and Physics*, *9*, 97–100.

Edelstein, W. A., Hutchison, J. M. S., Smith, F. W., Mallard, J., Johnson, G. and Redpath, T. W., 1981. Human whole-body NMR tomographic imaging: normal section. *British Journal of Radiology*, *54*, 149–151.

Holland, G. N., Moore, W. S. and Hawkes, R. C., 1980. NMR tomography of the brain. *Journal of Computer Assisted Tomography*, *4*, 1–3.

Hoult, D. I., 1977. Zeugmatography—a criticism of the concept of selective pulses. *Journal of Magnetic Resonance*, *26*, 165–167.

Mansfield, P., 1977. Multi-planar image formation using NMR spin echoes. *Journal of Physics, C*, *10*, L55–58.

Mansfield, P. and Maudsley, A. A., 1977. Medical imaging by NMR. *British Journal of Radiology*, *50*, 188–194.

Mansfield, P., Maudsley, A. A. and Baines, T., 1976. Fast scan proton density imaging by NMR. *Journal of Physics E*, *9*, 271–278.

Mansfield, P. and Morris, P. G., 1981. *NMR Imaging in Biomedicine*, Supplement 2 in the series *Advances in Magnetic Resonance* (Ed. by J. S. Waugh) (Academic Press, New York) (in press).

Mansfield, P., Morris, P. G., Ordidge, R. J., Pykett, I. L., Bangert, V. and Coupland, R. E., 1980. Human whole-body imaging and detection of breast tumours by NMR. *Philosophical Transactions of the Royal Society of London B*, *289*, 503–510.

Mansfield, P. and Pykett, I. L., 1978. Biological and medical imaging by NMR. *Journal of Magnetic Resonance*, *29*, 355–373.

Mansfield, P., Pykett, I. L., Morris, P. G. and Coupland, R. E., 1978. Human whole-body line-scan imaging by NMR. *British Journal of Radiology*, *51*, 921–922.

Sutherland, R. J. and Hutchison, J. M. S., 1978. Three dimensional NMR imaging using selective excitation. *Journal of Physics E*, *11*, 79–83.

Book reviews

Nuclear Medicine—Focus on Clinical Diagnosis. By Richard P. Spencer, pp. 291, 1980 (2nd edit.) (Medical Examination Publishing Co., New York), $18.00.
ISBN 0-87488-825-5

The first edition of this book, published in 1977, was clearly a success. It gave a broad and rapid view of clinical nuclear medicine without discussion of physics or radiopharmacy, and the second edition aims to do the same in a series of systematically arranged chapters, followed by a chapter on record-keeping and a glossary.

There is a wealth of information in this book but it is not always presented lucidly. The style is often colloquial and better fitted to the lectures on which the book was originally based. Although only three years have elapsed since the previous edition it is disappointing that the only readily detectable change is an increase in the number of pages. Omission of many historical events and techniques and better illustrations would have been an improvement. There are one or two errors of fact, such as the inaccurate legend to the radiograph Fig. 8.6; a misprint of "sufficient" for "insufficient" on page 125; and the use of "dye" for "contrast agent".

It is boring to reiterate earlier criticisms but a fuller integration of nuclear medicine techniques with other radiological techniques would be more welcome by readers in this country.

The chapter discussing record-keeping, etc., is more suited to legislation in the USA than the EEC but is nevertheless interesting and useful reading. There is the merit that the only mathematics quoted are found at the end of the book, rather than the traditional opening broadside.

Despite many valuable discussions and descriptions, the overall impact of the book is disappointing. The reason is perhaps found in the preface which indicates a dual use intended for the book, firstly as an initial text for residents in nuclear medicine, and secondly as part of the training programme in nuclear medicine technology. Such a dual aim cannot be attained successfully within one volume.

E. Rhys Davies.

Scintillation Camera Acceptance Testing and Performance Evaluation. By the Nuclear Medicine Committee of the American Association of Physicists in Medicine (AAPM) (AAPM Report No. 6) 22 pp., 1980 (American Institute of Physics (for AAPM), Chicago), $3.00.
ISBN 0-88318-275-0

This report, prepared by the Nuclear Medicine Committee of the American Association of Physicists in Medicine, is directed to users of nuclear imaging equipment and deals with proposed schemes for acceptance testing and performance evaluation of the scintillation camera. Since the test equipment necessary to do some of the performance measurements as laid down by the National Electrical Manufacturers' Association (NEMA) may not be available to every user, the report describes appropriate procedures of a more qualitative nature.

In addition to outlining methods of investigating temporal resolution, spatial and energy resolution, sensitivity, uniformity and shield leakage, the report recommends a protocol for electrical and mechanical safety inspection and the adoption of log books for tabulating performance, component failure and maintenance records. Those tests which yield numerical values for performance parameters comparable to NEMA specification are indicated in the text.

In general, the methods described are readily applicable by the user with a minimum of equipment although further discussion of those measurements suitable for regular routine quality control would have added to the usefulness of the report. Some indication of flood-field source dimensions (3.2.1) in relation to detector field of view and a figure illustrating a typical transmission bar phantom (4.1.1.4) would have been helpful.

In summary, however, this modestly priced publication should be of assistance to those users with little or no digital equipment who wish to undertake their own acceptance testing and performance evaluations.

M. Short.

the screening cost is likely to be of the order of £3 per screen by mammography (Mooney and Scott, 1978), giving a total cost of £3 million per annum for each group of women screened. (The treatment costs should of course also be included but tend to be small in relation to screening costs.)

Introducing these costs puts a different complexion on the issue, because in deciding who to screen we now have to form an explicit judgment of what monetary value we will attach to human life. Thus is it worth spending £30 million (£3 million for, say, ten years) to save 11 lives of women aged 55–59; or more brutally is the value of a woman aged 55–59 more than £2.7 million? Is it worth spending £15 million (£3 million for five years) to save 41 lives of women aged 60–64; or is the value of a woman aged 60–64 more than £370000?

We can complicate the analysis further in two ways:

(a) by proposing an asymmetry in values, *i.e.* that a death avoided is valued at less than a death "created" (possibly reflecting the view that the health service cannot be seen to be doing harm—even if it is also doing good; perhaps most apparent in society's attitudes to adverse drug reactions);

(b) by allowing for "discounting", *i.e.*, deaths postponed are better than deaths now.

The effect of (a) would be to increase the costs of deaths "created", thereby increasing total costs from screening, and in turn requiring even higher values of life for lives saved to justify mammography in breast cancer screening; the effect of (b) would be to decrease the costs of deaths "created" since these are likely to occur later than deaths avoided, thereby requiring lower values to justify mammography in breast cancer screening. Since both the asymmetry and the rate of discounting involve an element of judgment, we have further reason to see why judgments as to whom to screen are extremely difficult. (On the basis of Bailar's figures, I would form the judgment that no one should be screened by mammography annually over a lifetime for breast cancer since asymmetry, in my judgment, is more powerful than discounting, and consequently I would need to place a value of more than £400000 on the life of a woman aged 60–64 before being able to argue in favour of annual mammography in screening for breast cancer.)

CONCLUSION

What this paper has attempted to do is to emphasize:

(i) the importance of the cost-benefit approach to decision-making on resource allocation in those areas of activity in which life enters as a benefit, or loss of life as a cost;

(ii) the problems surrounding the issue of who is to do the valuing of such matters as life and death, and risk and benefit; and

(iii) in the context of screening for breast cancer and the ICRP recommendations that resource costs matter, and that valuing human life and risks thereto cannot and should not be avoided.

REFERENCES

BAILAR, J. C., III, 1977. Screening for early breast cancer: pros and cons. *Cancer*, *39*, *Supplement*, 2783–2795.

BRESLOW, L., HENDERSON, B., MASSEY, F. JR., PIKE, M. and WINKELSTEIN, W. JR., 1977. Report of NCI *ad hoc* working group on the gross and net benefits of mammography in mass screening for the detection of breast cancer. *Journal of the National Cancer Institute*, *59*, 474–478.

DRUMMOND, M. F., 1980. *Principles of Economic Appraisal in Health Care.* (Oxford University Press, London).

ICRP, 1977. *Recommendations of the International Commission on Radiological Protection.* ICRP Publication 26. (Pergamon Press, Oxford).

JONES-LEE, M. W., 1976. *The Value of Life. An Economic Analysis.* (Martin Robertson, London).

MOONEY, G. H., 1977. *The Valuation of Human Life.* (Macmillan, London).

MOONEY, G. H. and SCOTT, A. M., 1978. *Cost-Effectiveness of Breast Cancer Screening.* University of Aberdeen, HERU Discussion Paper, 02/78.

SINCLAIR, T. C., 1969. Costing the hazards of technology. *New Scientist*, October 16.

SINCLAIR, T. C., MARSTRAND, P. and NEWICK, P., 1972. *Human Life and Safety in Relation to Technical Change.* University of Sussex, Science Policy Research Unit.

WILLIAMS, A., 1974. The cost benefit approach. *British Medical Bulletin*, *30*, 252–6.

1981, *British Journal of Radiology*, *54*, 866–869

Ultrasound features of tumour thrombus in the IVC in retroperitoneal tumours

By S. J. Pussell, F.R.A.C.P. and D. O. Cosgrove, M.R.C.P.

Department of Nuclear Medicine and Ultrasound, Royal Marsden Hospital, Downs Road, Sutton,
Surrey SM2 5PT

(*Received October 1980 and in revised form April 1981*)

ABSTRACT

Tumour invasion of the inferior vena cava (IVC) is a complication of retroperitoneal tumours that can be identified at the time of ultrasound B scanning. We have recognized nine patients with proven IVC tumour thrombus from such tumours and have noted several common ultrasound features. Six of these cases were associated with renal carcinoma, two with metastatic teratoma and one with rhabdomyosarcoma. The typical appearance included abnormal echogenic solid material in the lumen of the vessel. In sagittal section the anterior wall was domed as it stretched over the thrombus, and on real time scanning there was loss of the normal venous pulsations. Although similar abnormalities occur with non-tumour thrombus, the presence of these typical features in association with a retroperitoneal tumour is likely to represent tumour invasion of the IVC, an important observation for accurate staging and subsequent management.

Tumour invasion of the inferior vena cava (IVC) is a well recognized complication of renal carcinoma. It also occurs with other retroperitoneal tumours. Ultrasound has been used successfully in assessing the IVC for extension of tumour from renal carcinoma (Goldberg *et al.*, 1978; Goldstein *et al.*, 1978; Greene and Steinbach, 1975; Harris, 1976) and indeed for the mass effects of other nearby tumours (Gosink, 1978, Kurtz *et al.*, 1979). This small series describes some of the ultrasound features of tumour thrombus in the IVC associated with retroperitoneal tumours.

PATIENTS AND METHODS

Patients were examined with a non-commercial, high-resolution grey-scale B scanner at 3.5 MHz and more recently also with the EMI 4500 Emisonic real time scanner. In this series of nine patients with tumour invasion of the IVC, five were due to renal carcinoma of the right kidney, one due to renal carcinoma of the left kidney, two were associated with teratoma with massive para-aortic lymphadenopathy and one with rhabdomyosarcoma of the right psoas muscle. The final diagnosis of tumour thrombus in the IVC was reached by surgery or autopsy in five cases and was concluded in four cases on clinical grounds together with venogram or X-ray computed tomography confirmation. In only three cases was there clinical evidence of venous thrombus with bilateral leg oedema and/or pulmonary emboli.

Once the diagnosis of tumour thrombus in the IVC had been reached, the ultrasound images were reviewed. Common morphological changes in the vessel and the features of the echo content were noted (Table I).

RESULTS

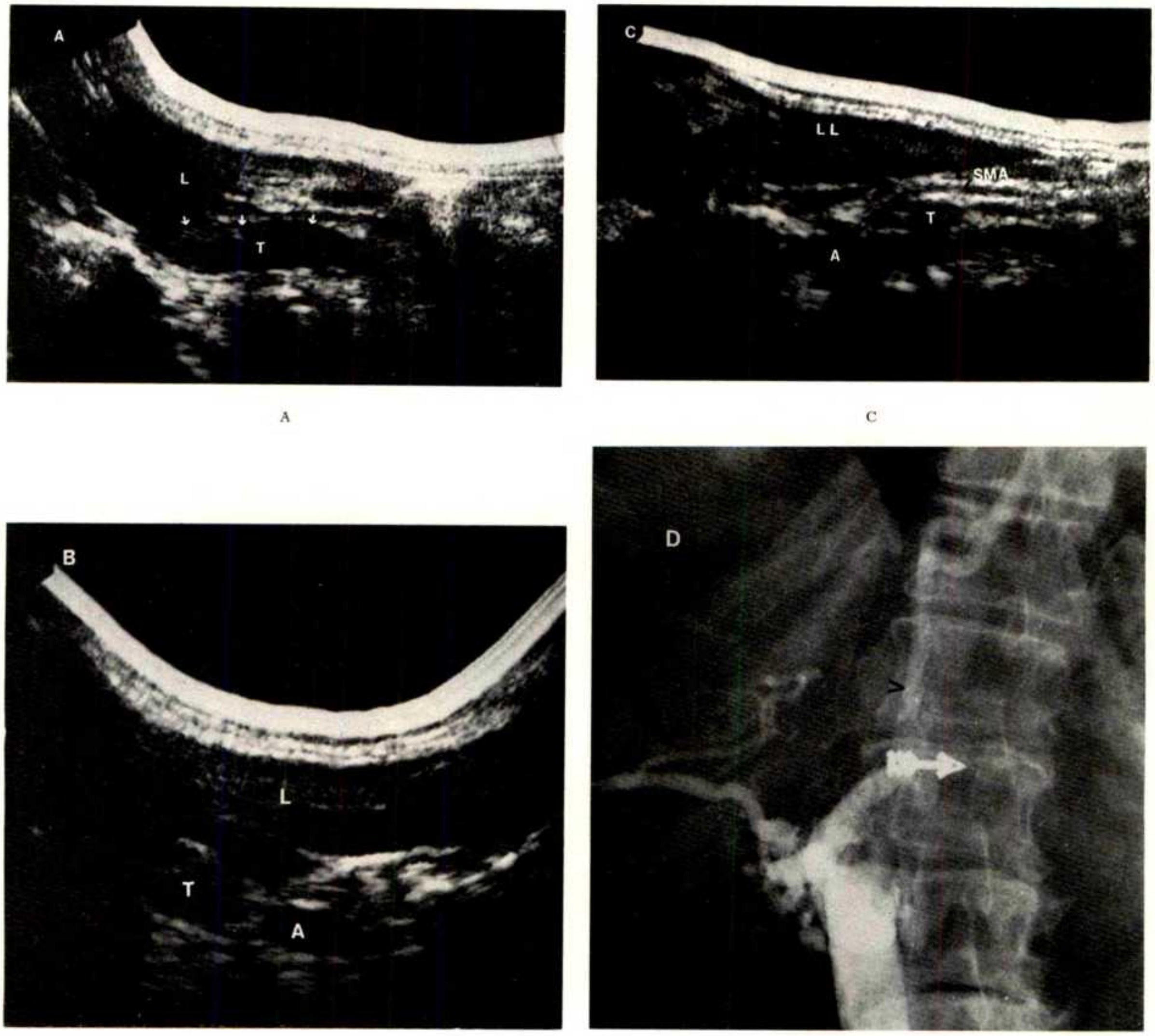
Several features were common to all nine cases. All were recognized because of an abnormality in the upper abdominal IVC at the level of the liver. The echo amplitude of the intraluminal thrombus was equal to or higher than that of the liver in all cases (Figs. 1–5). The echo content was homogeneous in five cases. Two cases had an inhomogeneous pattern but with predominantly high level echoes (Figs. 3, 4).

The shape of the vessel was altered in all cases. Distension was judged present when the shape of the vessel in transverse section was altered from the normal flattened appearance to a more rounded shape as occurs in congestive heart failure (Fig. 1B). This was seen in all but one patient who had an asymmetrical enlargement of the vessel which was partially filled with thrombus (Fig. 3B). In six cases the vessel was also enlarged (Figs. 2, 3). There was a typical appearance in the sagittal section (Figs. 1A, 2A, 3A). The posterior wall was relatively unaltered while the anterior wall was domed as it stretched over the thrombus. The lumen could not be recognized in four cases and these were the most difficult to diagnose (Figs. 1B, 5). More recently real time scanning has enabled detection of venous pulsations and helped to locate thrombus in the lumen.

TABLE I

ULTRASOUND FEATURES OF TUMOUR THROMBUS

Upper abdominal IVC shows:
Echogenic solid material in lumen Enlargement and distension Domed anterior wall Absent pulsations (real time)

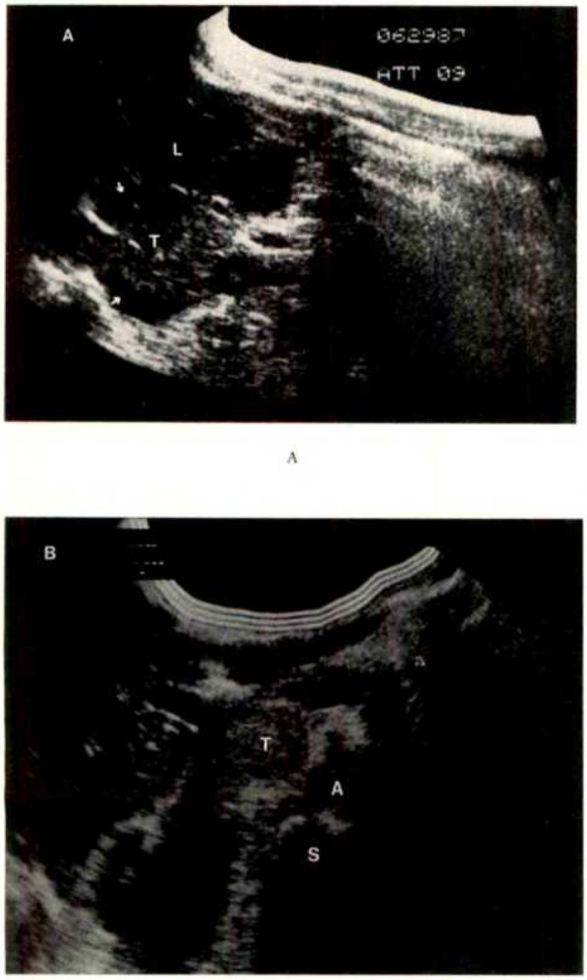


A C

B D

FIG. 1.

Left renal cell carcinoma. (A) Sagittal section through the liver (L) and IVC which is filled with tumour thrombus (T). Note the echogenic solid material filling the lumen and the domed anterior wall of the vessel. (B) Transverse section through the liver (L). The aorta (A) lies to the left of the tumour-filled, distended IVC (T). (C) Left sagittal section through the left lobe of the liver (LL) and the aorta (A). The superior mesenteric artery (SMA) can be seen passing over tumour thrombus (T) in the left renal vein which is completely filled and distended. (D) IVC venogram showing a complete obstruction at the upper border of L2 vertebra. The white arrow indicates the level of the xiphi-sternum. Contrast medium is shown in the azygos vein (black arrow).



A

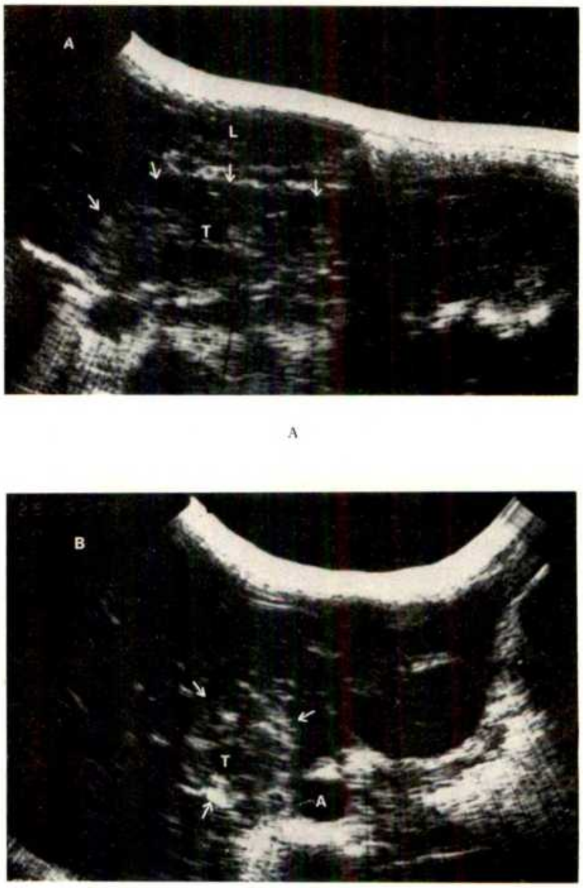
B

Fig. 2.

Right renal cell carcinoma. (A) Sagittal section with tumour thrombus (T) in the IVC. Part of the lumen can be seen (arrows). Liver (L) lies anteriorly. (B) Transverse section through the upper abdomen showing the IVC completely filled with homogeneous echogenic solid material (T). Note the distension and enlargement. The aorta (A) lies to the left in front of the spine (S).

Discussion

Certain ultrasound features are common to all these cases of tumour extension to the IVC from the retroperitoneal area. Some of these features are not pathognomonic of tumour but can also occur with venous thrombosis in this and other vessels. Distension and contained solid material have been shown to occur with non-malignant thrombus (Azimi *et al.*, 1978; Fowler and Paciulli, 1978). Since patients with malignancies have an increased tendency to thrombosis, the distinction between tumour and non-tumour thrombus is most important for proper staging and management. Often this distinction will not be possible by ultrasound even with sophisticated tissue characterization methods because of a small tumour component to the thrombus in some cases. In this situation all imaging techniques will fail to make the distinction. If tumour is the predominant component then enlargement of the vessel can also be expected and the diagnosis made with more confidence. This is true also for CT and venography (Holtz and Powers, 1962; Steele *et al.*, 1978).



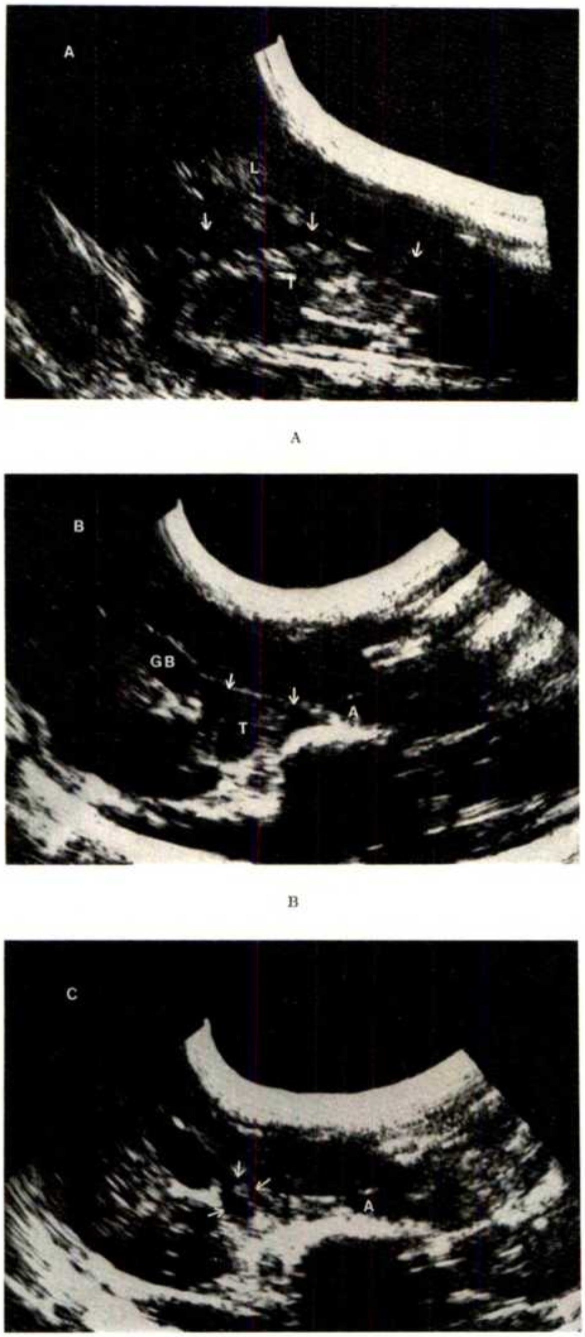
A

B

Fig. 3

Rhabdomyosarcoma of right psoas muscle. (A) Sagittal section showing the grossly enlarged IVC with domed anterior wall (arrows) filled with heterogeneous echogenic solid tumour (T). (B) Transverse section through the liver showing the tumour (T) within the asymmetrically enlarged IVC (arrows) just to the right of the aorta (A).

Regardless of these difficulties, if all the ultrasound features described here are found in a patient with retroperitoneal tumour, then there is a high



A

B

C

FIG. 4.

Teratoma. (A) Sagittal section through the liver (L) and IVC. The lumen is partially patent (arrows) but tumour thrombus (T) almost completely fills the vessel. The thrombus appears as heterogeneous echogenic solid material. (B) Transverse section. The partially tumour (T) filled lumen (arrows) is shown between the gall bladder (GB) and the aorta (A). (C) Transverse section. A tongue of solid material can be seen projecting into the lumen of the IVC (arrows). The aorta (A) lies to the left.

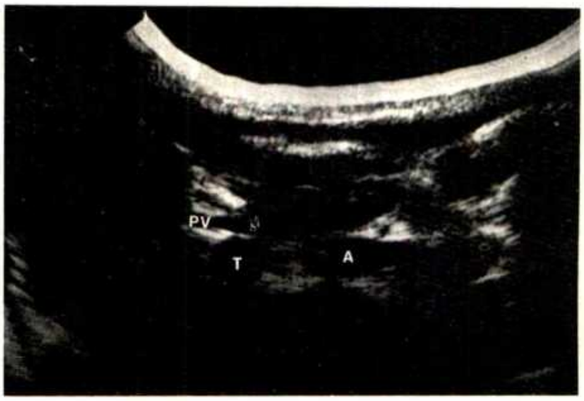


FIG. 5.

Right renal carcinoma. Transverse section. Tumour thrombus in the IVC (T) appears as homogeneous solid material with echo amplitude equal to the liver. The portal vein (PV) lies anteriorly and the aorta (A) to the left.

level of suspicion of tumour invading the IVC. Conversely, these features should be sought in all cases of retroperitoneal tumour by a careful assessment of IVC patency.

ACKNOWLEDGMENTS

We are grateful to EMI Medical for the provision of the real time machine that was used in this study. Dr. S. J. Pussell acknowledges the support of the Coppleson Postgraduate Medical Foundation, Australia.

REFERENCES

AZIMI, F., MARANGOLA, J. P. and KIRCH, K. H., 1978. Ultrasonic diagnosis of tumour thrombosis of right renal vein. *Urology*, *12*(*1*), 106–107.

FOWLER, J. E. and PACIULLI, J., 1978. Renal vein thrombosis: Diagnosis by B-Scan ultrasonography. *Journal of Urology*, *118*, 849–850.

GOLDBERG, B. B., PATEL, J. and POLLACK, H. M., 1978. Evaluation of renal tumours. In *Ultrasound in Tumour Diagnosis*, Eds. C. R. Hill, V. R. McCready, D. O. Cosgrove (Pitman Medical, Tunbridge Wells), pp. 162–198.

GOLDSTEIN, H. M., GREEN, B. and WEAVER, R. M. J., 1978. Ultrasonic detection of renal tumour extension into the inferior vena cava. *American Journal of Roentgenology*, *130*, 1083–1085.

GOSINK, B. B., 1978. The inferior vena cava: Mass effects. *American Journal of Roentgenology*, *130*, 533–536.

GREENE, D. and STEINBACH, H. L., 1975. Ultrasonic diagnosis of hypernephroma extending into the inferior vena cava. *Radiology*, *115*, 679–680.

HARRIS, R. D., 1976. The etiology of inferior vena cava obstruction. *CRC Critical Reviews in Diagnostic Imaging*, *8*, 57–86.

HOLTZ, S. and POWERS, W. E., 1962. Inferior venacavograms. *Radiology*, *78*, 583–590.

KURTZ, A. B., RUBIN, C. and GOLDBERG, B. B., 1979. Ultrasound diagnosis of masses elevating the inferior vena cava. *American Journal of Roentgenology*, *132*, 401–406.

STEELE, J. R., SONES, P. J. and HEFFNER, L. T., 1978. The detection of inferior vena caval thrombosis with computed tomography. *Radiology*, *128*, 385–386.

1981, *British Journal of Radiology*, *54*, 870–874

An appraisal of the use of diagnostic ultrasound to quantify the lumbar spinal canal

By *‡D. Finlay, F.R.C.R., †H. R. Stockdale, Ph.D. and *E. Lewin, D.M.U.

*X-ray Department, University Hospital, Nottingham and
†Medical Physics Department, City Hospital, Hucknall Road, Nottingham

(*Received January 1981 and in revised form May 1981*)

ABSTRACT

Performing an ultrasound scan of the lumbar spine produces a multitude of backscattered echoes from the bony structures between the transducer and the vertebral structures. We present *in vitro* evidence to demonstrate the potential sources of uncertainty.

The use of diagnostic pulse echo ultrasound to measure the spinal canal has recently been proposed (Porter *et al.*, 1977; 1978b). Other papers describing both specific applications of this technique and more generalized aspects of the role of ultrasound measurements in the clinical management of low back pain have been presented (Porter *et al.*, 1978a; 1980a; 1980b). Few other authors have commented on this technique and their comments generally do not share the initial enthusiasm (Hawkes and Roberts, 1980; Park, 1980; Stockdale and Finlay, 1980; Veiga-Pires *et al.*, 1981). However, a response in favour of this application has been given (Ottewell and Howells, 1981).

We wish to discuss in rather more detail the logistics of scanning the lumbar spinal canal. The role of this procedure in clinical practice is not of immediate concern in this paper but we feel entitled to make a few generalizations regarding the consequences of not being able to resolve any or all of the potential artefacts that we shall describe.

MATERIALS AND METHODS

In order to clarify some of the unusual results that we have reported elsewhere (Stockdale and Finlay, 1980) we embarked on a series of *in vitro* experiments in order to highlight the origins of any potential artefacts.

1. In vitro *work*

Two dried lumbar vertebrae (L_4 and L_5) were fastened together with a plasticine insert of about 1 cm thickness between them. The vertebrae were submerged in distilled water with the transducer inclined at 15° to the lumbar axis (Fig. 1). The ultrasound machine used was a Nuclear Enterprises 4200 Diasonograph with a transducer of nominal frequency 2.25 MHz (13 mm diameter, long internal focus).

B-scan images were produced across the oblique sagittal dimension by both linear and compound scanning. These scanning techniques are well

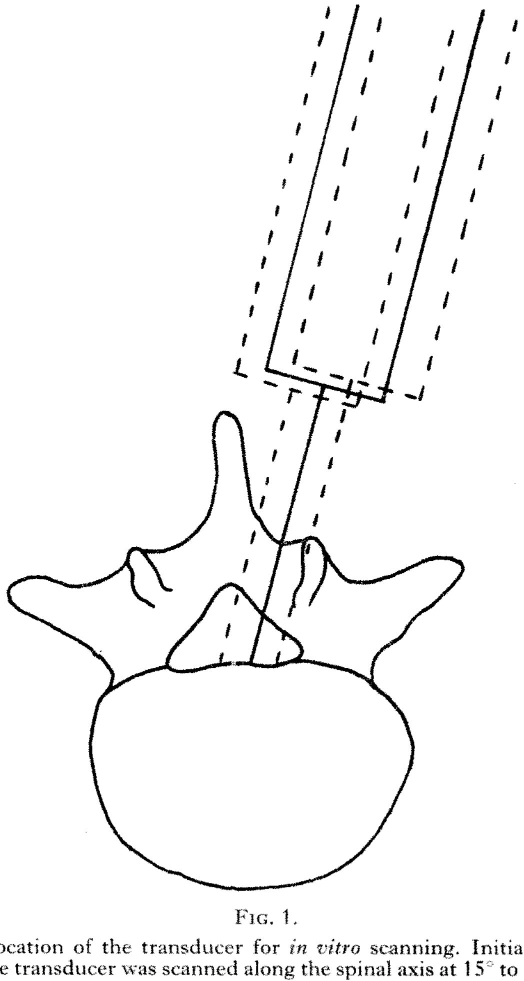


FIG. 1.

Location of the transducer for *in vitro* scanning. Initially, the transducer was scanned along the spinal axis at 15° to the sagittal plane with the transducer located visually over the middle portion of the lamina (solid line). Subsequent scans were similarly generated but with the transducer moving in a plane either 4 mm more laterally or 4 mm more medially than the original plane (dashed lines).

---

‡Present address: X-ray Department, Royal Infirmary, Leicester.

Reprint requests: Dr. Stockdale.

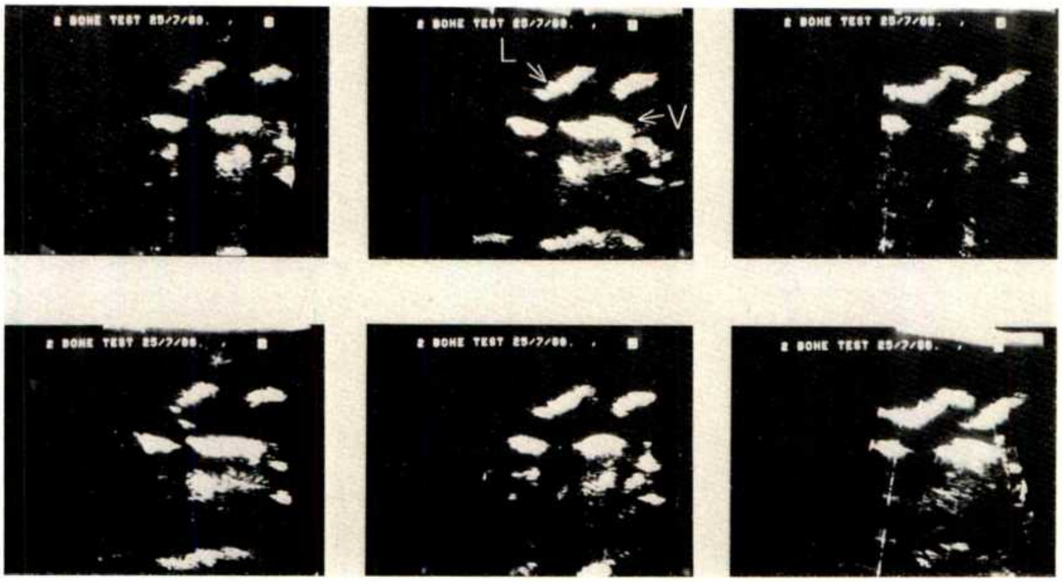


FIG. 2.

Typical *in vitro* B-scan images. The upper row is generated by linear scanning and the lower by compounding. The middle column was obtained with the transducer in the mid-position shown in Fig. 1. The column on the left was obtained by moving the transducer 4 mm more medially whilst that on the right was obtained by moving the transducer 4 mm more laterally. L represents the image from the posterior lamina surface. V represents the image from the posterior vertebral body surface.

described elsewhere (Shirley *et al.*, 1978). Similar scans were also produced both at 4 mm more lateral and at 4 mm more medial to that plane (Fig. 1). The images that were produced are obviously not identical but they do contain the same basic features, that is, the posterior lamina surface and the posterior surface of the vertebral body (Fig. 2). Note the apparent difference in the canal dimensions when using different scanning planes. Moving the plane more laterally appears to reduce the canal gap on the B-scan.

From the linearly generated images, it is clear that negligible transmission of ultrasound through the lamina is seen since there is only a small amount of overlap between the reflections from the lamina and its vertebral body. Some overlap will be produced due to the finite width of the interrogating ultrasound beam. Consequently, transmission of ultrasound through the lamina as described by Porter *et al.*, (1978b) is doubtful. The increased overlap of the lamina and the vertebral body when compound scanning is compared with linear scanning is a result of rocking the transducer. The problem associated with choosing the appropriate scanning plane is considered by us to be one of the major factors determining the confidence one can place in the *in vivo* procedure.

The question of deciding which A-scan peaks correspond to which of the various anatomical structures is not trivial. One observes a broad composite echo (Fig. 3) moving in a manner defined by the lamina's posterior surface contours when moving the transducer along the spinal axis. Due to the ultrasound beam width, this composite echo will be made up of reflections from either facet joints or posterior spinal processes depending on the precise location of the scanning plane. Of the individual echoes making up this composite echo, the reflection off the more anterior edge of lamina that probably needs to be used to quantify the spinal canal will be the one occurring latest in time. It is well known that ultrasound measurements require that the two caliper pips which define the distance being quantified need to be located on the start of the leading edge of the A-scan peak (McDicken, 1976; Shirley *et al.*, 1978). The leading edge of the lamina echo may be lost in the other echoes making up this composite echo. The leading edge of the echo from the posterior surface of the vertebral body can usually be picked out with adequate confidence.

The achievement of a unique definition of the lateral displacement of the transducer by searching for echoes of equal amplitude has been suggested by Ottewell and Howells (1981). However, such echoes

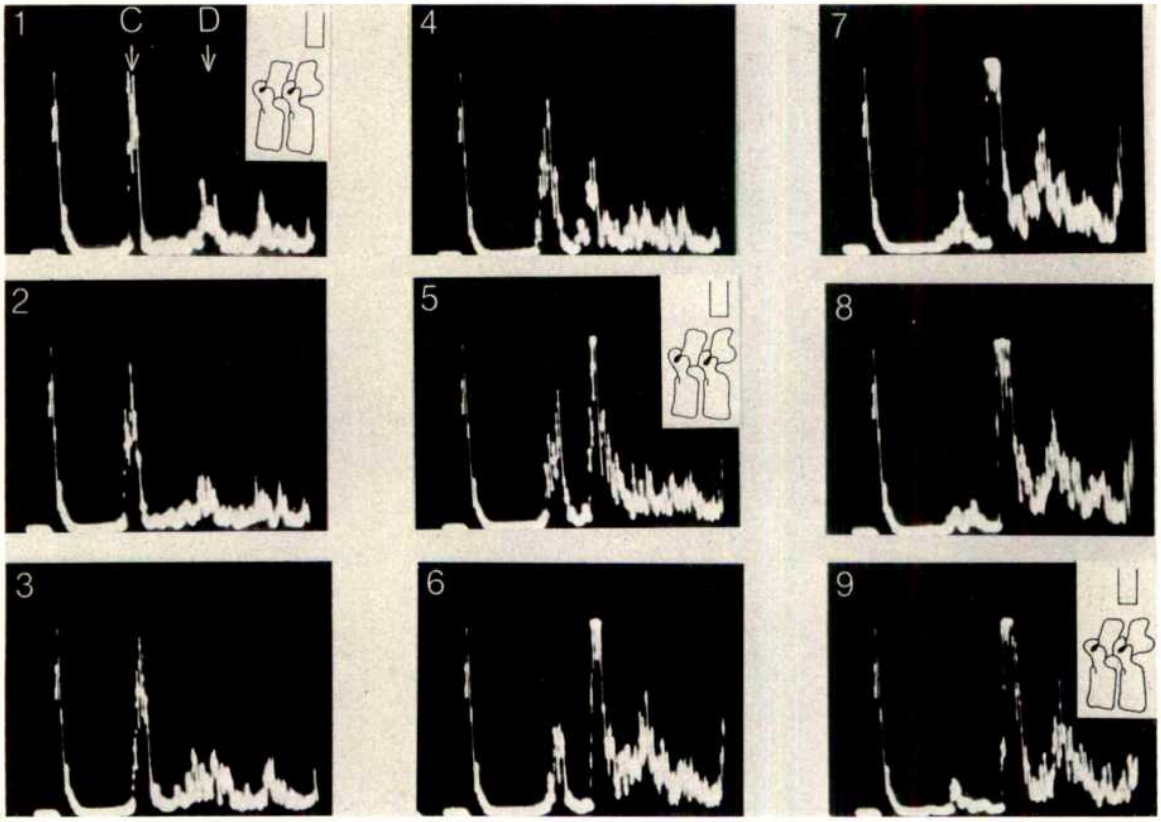


FIG. 3.

In vitro A-scan echo patterns produced when moving the transducer along the mid-position shown in Fig. 1. The composite echo (C) moves in time corresponding to the posterior surface contours of the lamina. The echo marked D arises from the posterior surface of the vertebral body. The photographs were taken at 2 mm intervals along the spinal axis. Photograph 1 was taken with the transducer located over the most posterior aspect of the lamina. Photograph 5 shows the ultrasound beam intercepting both the anterior lamina edge and the posterior margin of the vertebral body. Photograph 9 was taken with the transducer located between adjacent laminae with no significant echo from either lamina and a dominant echo from the posterior margin of the vertebral body.

can be generated from the same canal space by moving the transducer either laterally in a fixed location along the spine or along the spinal axis in a fixed lateral plane. This phenomenon can be seen by looking at the "A" scans generated at the two extreme positions of the transducer shown in Fig. 1. These A-scans are shown in Fig. 4. The echoes of equal amplitude shown in frame 4 (or 5) of Fig. 3 could be confused with those displayed in frames M2 and L4 in Fig. 4.

Therefore, even in this rather simplified arrangement of dried bones suspended in water, there is still a problem of reliably quantifying that which at best is selected somewhat subjectively. Measuring from the trailing to the leading edge across changes in acoustic impedances can lead to errors in the recorded dimension. The magnitude of these errors will be a function of the electronic processing within the ultrasound machine and cannot be reliably estimated but could lead to reductions in the measured dimension of possibly a few millimetres.

2. In vivo *work*

Bearing in mind our observations from the *in vitro* studies, we must comment on the *in vivo* use of this technique. We feel that three potential problems exist. Firstly, one has to select the appropriate scanning plane; secondly, one has to identify reliably the A-scan peaks and thirdly, one has the difficulty of deciding where to locate the caliper pips on the echo pattern. Any one of these problems, unless satisfactorily resolved, is capable of giving artefactual results. Whether it is possible to eliminate these problems by improving the scanning technique is debatable. Admittedly, a good knowledge of orthopaedic anatomy and a sound understanding of the

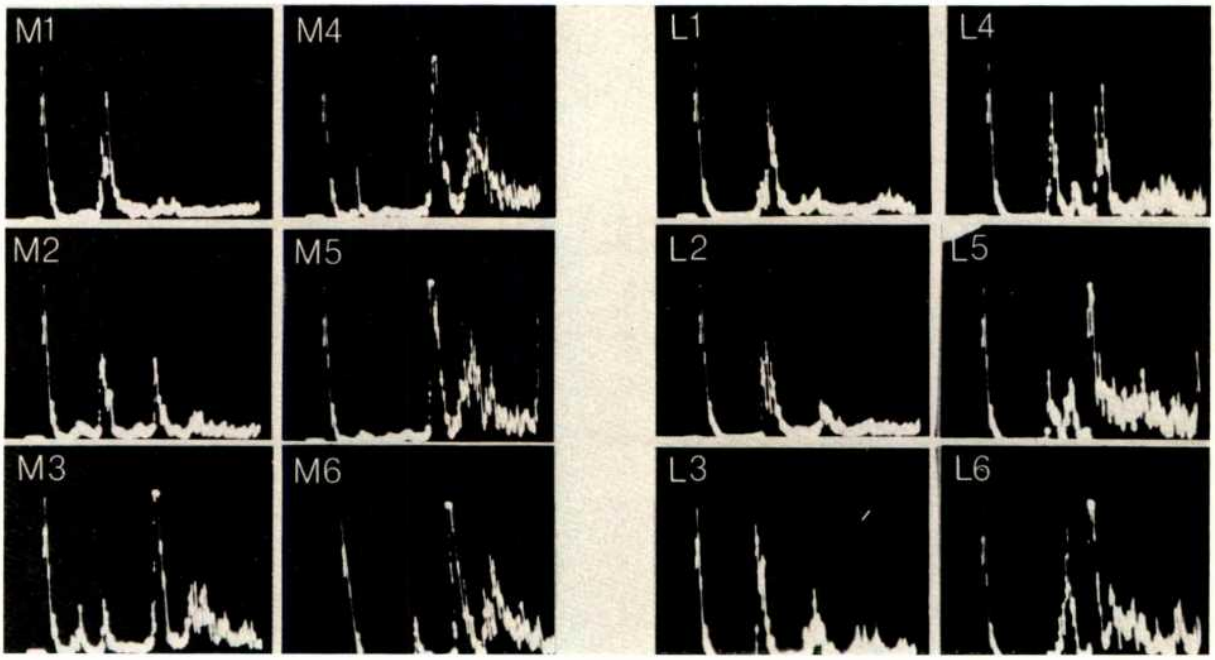


FIG. 4.

In vitro A-scan echo patterns produced when moving the transducer along the more lateral (L) and more medial (M) planes shown in Fig. 1. The photographs were taken at 4 mm intervals along the spinal canal. M1 (and L1) were taken with the transducer located over the most posterior aspect of the lamina. M6 (and L6) were taken with the transducer located between adjacent laminae. (L6 contains additional echoes, possibly originating from facet joints.)

physics of ultrasound mensuration will help diminish these problems but nevertheless, problems will still remain.

One could perhaps carry out a comparative trial in order to assess either intra- or inter-observer variability. However, should two operators apply the same subjective criteria when selecting the scanning plane or perhaps, identifying the echoes from a particular plane, then a meaninglessly small inter-observer discrepancy would be recorded.

CONCLUSION

We feel that the use of diagnostic ultrasound to quantify the spinal canal is novel and worthy of note. However, we feel bound to highlight those areas in which we consider that problems exist. Clearly, more investigations need to be made in the acoustic interactions occurring within the lumbar spine.

It should be added that two classes of results are possible. Firstly, the canal dimension at each vertebral level could be similar for a particular individual. The implication from such a result is that either the expected oblique sagittal dimension is being assessed or that due to incorrect selection of the scanning plane, all the results are artefactually high or low. In our opinion, which of these two situations is actually the case cannot be known at present.

Secondly, the canal dimensions at each level could be irregular and unpredictable. From such a result, one may be recording true canal anatomy, or perhaps, due to incorrect echo selection and/or incorrect placement of the pips, one may merely be recording meaningless and inappropriate lengths. Again, in our opinion, which of these options is actually occurring is indeterminate at present.

ACKNOWLEDGMENTS

We wish to record our thanks for the advice and encouragement given by the following people: Mr. R. C. Mulholland, Consultant Orthopaedic Surgeon, Dr. P. Davies, Consultant Radiologist, and Miss R. E. Richardson, Senior Physicist. Also we appreciate the help given by all the staff of the X-ray Department, University Hospital, Nottingham.

REFERENCES

HAWKES, C. H. and ROBERTS, G. M., 1980 Lumbar canal stenosis. *British Journal of Hospital Medicine* (May), 498–505.

MCDICKEN, W. N., 1976. *Diagnostic Ultrasonics—Principles and Use of Instruments.* (Crosby Lockwood Staples, London).

OTTEWELL, D. and HOWELLS, P., 1981. The use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *54*, 430.

PARK, W. M., 1980. Radiology in the investigation of low back pain. *Clinics in Rheumatic Diseases*, *6*, 93–132.

PORTER, R. W., HIBBERT, C. and WELLMAN, P., 1980a. Backache and the lumbar spinal canal. *Spine*, *5*, 99–105.

PORTER, R. W., HIBBERT, C., WELLMAN, P., LANGTON, C. and MILLINGTON, A., 1980b. The shape and size of the lumbar spinal canal. In *Engineering Aspects of the Spine* (Proceedings of a Meeting held at Institute of Mechanical Engineers, London, May 1980). (Mechanical Engineering Publications Ltd., London).

PORTER, R. W., HIBBERT, C. S. and WICKS, M., 1978a. The spinal canal in symptomatic lumbar disc lesions. *Journal of Bone and Joint Surgery*, *60B*, 485–487.

PORTER, R. W., OTTEWELL, D. and WICKS, M., 1977. Measurement of the lumbar spinal canal by diagnostic ultrasound. In *Orthopaedic Engineering* (Proceedings of a Meeting held in Oxford, September 1977) Ed. by J. D. Harris and K. Copeland (The Biological Engineering Society, London).

PORTER, R. W., WICKS, M. and OTTEWELL, D., 1978b. Measurement of the spinal canal by diagnostic ultrasound. *Journal of Bone and Joint Surgery*, *60B*, 481–484.

SHIRLEY, I. M., BLACKWELL, R. J., CUSICK, C., FARMAN, D. J. and VICKERY, F. R., 1978. *A User's Guide to Diagnostic Ultrasound.* (Pitman Medical Publishing Co. Ltd., Tunbridge Wells).

STOCKDALE, H. R. and FINLAY, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101–1102.

VEIGA-PIRES, J. A., BEEK, R. v. D. and KAISER, M. C., 1981. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *54*, 269.

Book review

Lumbale Myelographie mit wasserlöslichen Kontrastmitteln (*Lumbar myelography with water-soluble contrast media*). By M. Langlotz, pp. x+279 391 illus., 1981. (Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin (Advances in the field of X rays & nuclear medicine): Diagnostik, Physik, Biologie, Therapie. Ergänzungsband 109 (Supplementary Vol. 109)) (Georg Thieme, Stuttgart/New York), DM.178.
ISBN 3-13-5876-01-2

The revival of interest in water-soluble preparations for use in myelography was hastened by the introduction during the last ten to 15 years of new and safer products for use in this important investigation. They have proved of particular value in lumbar myelography and although much had been written in the literature it appeared as isolated reports of experiences or communications about small groups, or even single cases.

Dr. Michael Langlotz in Zürich has had a very extensive experience of the the use of this method and it is indeed good that he has taken it on himself to summarize a lot of what has appeared in the literature, and also to draw on his wide personal knowledge and collection of films.

The book is divided into two parts, the first 45 pages being a discussion of the theory of the procedure with sections on anatomy, the materials available with a history of their use, and discussions of the normal and the pathological myelogram. The technique of the procedure is discussed in detail so that the veriest beginner can benefit. Post-myelography management is described and there is a good account of artefacts and how to avoid them. The value of the various oblique views as well as erect films with a horizontal beam is emphasized, especially in the diagnosis of disc lesions, including far lateral foraminal ones.

There are separate chapters on malformations, herniated discs, stenosis of the lumbar canal, and tumours, as well as an account of the appearances and artefacts which may be encountered in a post-operative myelogram. There is an extensive bibliography comprising a total of 334 entries, grouped for ease of reference under each chapter heading. There are, for example, 63 papers on lumbar canal stenosis and 83 on the "post-operative" myelogram.

Tomography is regarded as unnecessary in most cases, except occasionally as a confirmatory measure. It was actually done in about ten per cent of cases and proved of value for (i) showing the conus, (ii) occult dysraphism, (iii) changes in the nerve roots and vessels in their course in the dural sac and (iv) bony stenosis in the differential diagnosis from disc herniation. Although not mentioned in this monograph it is likely that CT scanning will replace certain specialized techniques for the solution of some atypical problems.

The second part of the book first shows the normal anatomy and afterwards provides a comprehensive atlas of all the various conditions. In the section on normal anatomy there are some splendid radiographs of macerated specimens of the lumbar spine and of individual vertebrae, which will be of immense value for teaching. The value of the atlas is certainly enhanced by the excellent reproduction of the films, in their original size. There are more than 200 pages, with the films reproduced on the right-hand page and a summary of the clinical history on the left-hand page. The quality of the whole book is such as we have learned to expect from Thieme Verlag.

The pictures are so superb that this "Atlas" should be of value to all neuro-radiologists, even if they are not readers of German. It is a pleasure to handle and will be a valuable primer for beginners and an excellent reference book for experienced practitioners. It can be unreservedly recommended.

CHARLES LANGMAID.

1981, *British Journal of Radiology*, 54, 875–877 OCTOBER 1981

Monte Carlo calculation of the dose distributions across a plane bone-marrow interface during diagnostic X-ray examinations

By R. N. Kulkarni, M.Sc.

Division of Radiological Protection, Bhabha Atomic Research Centre, Bombay 400 085, India

(*Received August 1980 and in revised form March 1981*)

ABSTRACT

The distributions of dose across a plane bone-marrow interface on irradiation with various diagnostic X-ray beams at a representative site have been determined using the Monte Carlo method. The site was in a dorsal vertebra near its surface and situated at a depth of 70 mm under the skin. The X-ray beams studied were generated at 100, 90, 80 and 70 kV with 2 mm aluminium added filter and at 55 kV with 1 mm aluminium added filter.

It was found that the dose to bone marrow due to excess photoelectrons produced in bone falls off rapidly as the distance from the bone-marrow interface increases. Consequently, the percentage excess dose to a plane bone-marrow cavity, which is almost constant for the range of kV studied, is significant only if the cavity size is small.

Active or red bone marrow is contained in cavities between trabeculae in the spongy parts of bone. Since bone tissue consists of a larger percentage of elements with high atomic numbers, mainly calcium, it has a higher photoelectric cross-section than bone marrow. Consequently when the spongy part of a bone is irradiated, as during a diagnostic X-ray examination, with a beam of photons of energy up to 100 keV for which the photoelectric cross-section is significant, bone marrow near its interface with bone receives a higher dose than it would receive under electronic equilibrium conditions at sites remote from a bone surface.

It is now well established that leukaemia may be induced by irradiation of active bone marrow. The excess dose to bone marrow during irradiation with a low-energy photon beam has, therefore, interested many workers.

There is a very wide variety in the shapes and sizes of trabeculae and the marrow spaces between them (Spiers, 1968). It is, therefore, very difficult to calculate the dose distribution across a bone-marrow interface without some simplifying assumption regarding the interface. The usual shape of a bone-marrow cavity suggests that a cylindrical interface is generally a good assumption. Some trabeculae are, however, narrow plates and bars of bone (Johns and Cunningham, 1969). In such cases the interface can be assumed to be plane, without much inaccuracy. All the calculations of the dose distributions across bone-marrow interfaces on irradiation by photons have, therefore, been made in the past for plane or cylindrical interfaces. Early calculations have been made with further simplifying assumptions that secondary electrons travel in straight lines and lose energy at a uniform rate (Spiers, 1949, 1951; Munson, 1950; Woodard and Spiers, 1953). Charlton and Cormack (1962) first incorporated the variation of energy loss with electron energy fairly accurately during calculations for monoenergetic beams of photons. Aspin and Johns (1963) then made calculations for continuous X-ray spectra using the technique of Charlton and Cormack (1962). Charlton (1970) and Kulkarni *et al.* (1972) considered both the variation of energy loss and electron scattering. Charlton (1970) used the dose distributions due to point isotropic electron sources calculated by Spencer (1959) by the moments method. Kulkarni *et al.* (1972) showed how the dose distribution across a plane bone-marrow interface can be calculated using the moments method, independently of Spencer's (1959) results. However, while Charlton (1970) assumed equivalent distances in different materials, Kulkarni *et al.* (1972) assumed that bone and bone marrow are equivalent as far as electron scattering is concerned. These assumptions were eliminated by Sunderaraman and Prasad (1975) while using the Monte Carlo method to calculate the dose distribution across a cylindrical bone-soft tissue interface on photon irradiation. It was, therefore, considered desirable to calculate the dose distribution across a plane bone-marrow interface also using the Monte Carlo method. The distributions were determined for diagnostic X-ray beams generated at 100, 90, 80 and 70 kV with 2 mm aluminium added filter and at 55 kV with 1 mm aluminium added filter, at a representative bone marrow site, *viz.*, near the surface of a dorsal vertebra. The site was taken at a depth of 70 mm under the skin, because the surface of the dorsal spine is at about that depth (Ellis, 1961).

METHOD

The Compton coefficients per unit mass are almost equal in bone and soft tissue. Compton electrons, therefore, give almost the same dose to bone and bone marrow. In this work the contribution of excess photoelectrons produced in bone was computed using the Monte Carlo method. For this purpose the following procedure was adopted for every X-ray beam studied:

The region in bone marrow adjoining its interface with bone was divided into a number of slabs of equal thickness. For 70 kV X rays the slab thickness was 1/40 of the range of the most energetic secondary electrons and for other X-ray energies 1/10. Bone thickness was assumed to be sufficient to provide electronic equilibrium. This is the case for diagnostic X-ray beams (Spiers, 1968).

Four thousand histories were generated in bone up to the range of the most energetic secondary electrons. As in most of the earlier work it was assumed that the photon beam was perpendicular to the bone-marrow interface and that electrons were produced isotropically. Since an X-ray beam makes different angles with different interfaces, the above assumption can be expected to give more or less the average of the dose distributions in different cavities.

For sampling the initial energy of a photoelectron, its probability density function was needed. This function is the product of the relative photon intensity and the difference in photoelectric cross-sections in bone and bone marrow. Thus the photon energy spectra at a depth of 70 mm (at the site of interest) due to the different X-ray beams studied were needed. They were calculated using essentially the same Monte Carlo technique as used by Bruce and Johns (1960). The incident spectra of the different X-ray beams were taken from Epp and Weiss (1966). The initial energy, position and direction of the electrons were sampled on the basis of their respective probability distributions.

The artificially-constructed condensed random walk of the electron was then tracked by the method described by Berger (1963). Each step of such a walk takes into consideration the cumulative effect of a large number of elastic and inelastic collisions undergone by the electron. The size of a step in these calculations was such that the energy of the electron would come down, on average, by a factor of $2^{-1/16}$. The continuous slowing-down approximation was used. Transverse displacements were neglected. As the secondary electrons in this work all have low energies (less than 100 keV) and this is a one-dimensional problem, these simplifications are not likely to have introduced any significant error (Berger, 1963).

RESULTS AND DISCUSSION

Figure 1 shows, as a typical example, the distribution of excess dose to bone marrow near a bone-marrow interface for a 70 kV X-ray beam with 2 mm aluminium added filter at a depth of 70 mm under the skin. This would be the average dose distribution in the dorsal spine during a chest (postero-anterior) examination. It can be seen from this figure that the excess dose extends only over a small fraction of the range of the most energetic secondary electrons. The dose distributions for 25 and 35 keV beams given in ICRU (1959) are also shown in the figure, because the effective energy of the 70 kV beam is 29.5 keV. It can be seen from the figure that the distributions for 25 and 35 keV beams are quite close to the distribution for the 70 kV beam but the latter extends farther because of the presence of higher energy photons.

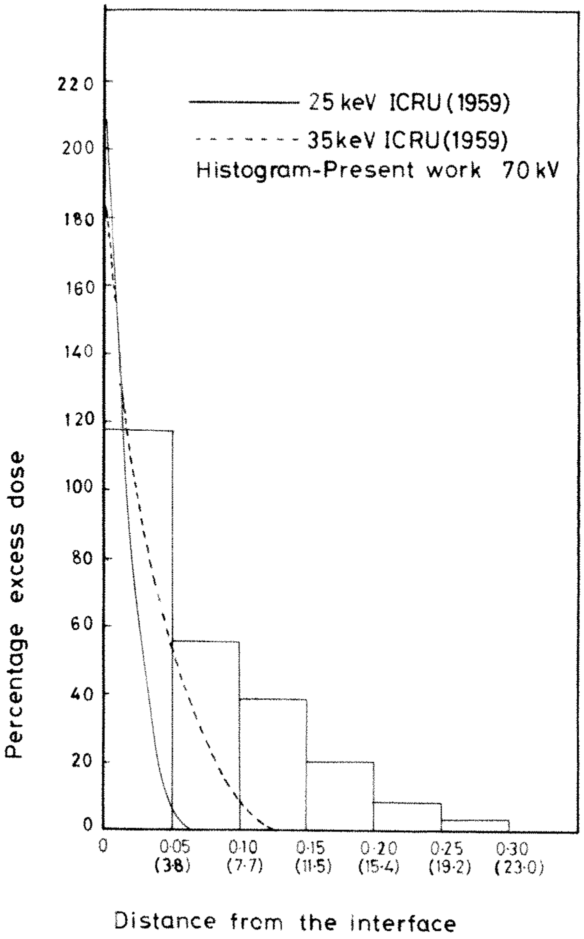


FIG. 1.

The distribution of excess dose to bone marrow near a plane bone-marrow interface. The distribution calculated in the present work is for an X-ray beam at 70 kV with 2 mm Al added filter, at a site near the surface of a dorsal vertebra, at a depth of 70 mm under the skin. The distance from the interface is in units of the range of an electron of energy 70 keV, and, in parentheses, in μm.

Since the dose to bone marrow due to excess photoelectrons in bone is received over only a small distance from the interface, the percentage excess dose to a cavity can be significant only if its size is small. The percentage excess dose to a plane cavity

TABLE I

PERCENTAGE EXCESS DOSE TO A PLANE BONE-MARROW CAVITY OF 200 μM THICKNESS AT A DEPTH OF 70 MM DUE TO SURROUNDING BONE

kV	Added filter	Half value Thickness mm Al*	Effective photon energy, keV†	Percentage excess dose ±standard deviation, this work	Percentage excess dose	
					ICRU (1959)	Jacobs and Spiers‡
100	2 mm Al	2.75	32	11.6±1.1	15	10.4
90	2 mm Al	2.5	31	9.8±0.9		
80	2 mm Al	2.3	30	9.9±0.8		
70	2 mm Al	2.1	29.5	9.0±0.7		
55	1 mm Al	1.4	25	8.8±0.6	10	6.9

**British Journal of Radiology Supplement 11*, Fig. 1.1, p.1.
†*British Journal of Radiology, Supplement 11*, Table C1, p. 107.
‡Quoted by Spiers (1968). Percentage excess doses are for a cylindrical cavity in the iliac crest.

of thickness 200 μm due to the different beams studied is shown in Table I. The values are almost equal for all the kVs. The reason, as can be seen from Table I, is that the effective energies of the different beams are very close. The percentage excess doses given in ICRU (1959) and by Jacobs and Spiers (quoted by Spiers, 1968) are also shown in Table I for comparison. The percentage excess dose to a plane marrow cavity of any size will be inversely proportional to the cavity size.

ACKNOWLEDGMENTS

The author wishes to thank Dr. S. J. Supe, Dr. P. S. Iyer and Mr. M. A. Prasad for valuable guidance. The interest evinced in this work by Dr. K. G. Vohra and Mr. G. Subrahmanian is also gratefully acknowledged.

REFERENCES

ASPIN, N. and JOHNS, H. E., 1963. The absorbed dose in cylindrical cavities within irradiated bone. *British Journal of Radiology*, *36*, 350–362.

BERGER, M. J., 1963. Monte Carlo calculations of the penetration and diffusion of fast charged particles. In *Methods in Computational Physics*, Vol. 1, Ed. B. S. Alder, M. Fernbach and M. Rotenberg, pp. 135–215. (Academic Press, New York).

BRITISH JOURNAL OF RADIOLOGY Supplement 11, 1978. *Central Axis Depth Dose Data for Use in Radiotherapy*. Ed. M. Cohen, D. E. A. Jones and D. Greene.

BRUCE, W. R. and JOHNS, H. E., 1960. Spectra of X rays scattered by low-atomic number materials. *British Journal of Radiology* Supplement 9.

CHARLTON, D. E., 1970. Energy dissipation near an interface. *Radiation Research*, *44*, 575–593.

CHARLTON, D. E. and CORMACK, D. V., 1962. Energy dissipation in finite cavities. *Radiation Research*, *17*, 34–49.

ELLIS, R. E., 1961. The distribution of active bone marrow in the adult. *Physics in Medicine and Biology*, *5*, 255–258.

EPP, E. R. and WEISS, H., 1966. Experimental study of the photon spectrum of primary diagnostic X rays. *Physics in Medicine and Biology*, *11*, 225–238.

ICRU, 1959. Report of the International Commission on Radiological Units and Measurements. National Bureau of Standards Handbook 78. (NBS, Washington, DC).

JOHNS, H. E. and CUNNINGHAM, J. R., 1969. *The Physics of Radiology*, 3rd Ed. (Charles C. Thomas, Springfield, Mass.)

KULKARNI, R. N., SUNDERARAMAN, V. and PRASAD, M. A., 1972. The dose across a plane bone-tissue interface. *Radiation Research*, *51*, 1–9.

MUNSON, R. J., 1950. A note on the paper of Spiers (1949). *British Journal of Radiology*, *23*, 505.

SPENCER, L. V., 1959. *Energy Dissipation by Fast Electrons.* National Bureau of Standards Monograph No. 1 (NBS, Washington, DC).

SPIERS, F. W., 1949. The influence of energy absorption and electron range on dosage in irradiation of bone. *British Journal of Radiology*, *22*, 521–533.

1951. Radiotherapeutic Physics II. Dosage in irradiated tissue and bone. *British Journal of Radiology*, *24*, 365–369.

1968. *Radioisotopes in Human Body: Physical and Biological Aspects.* (Academic Press, New York).

SUNDERARAMAN, V. and PRASAD, M. A., 1975. Dose distributions and mean doses in cylindrical cavities of bone marrow on X-ray irradiation. *Strahlentherapie*, *149*, 176–180.

WOODARD, H. Q. and SPIERS, F. W., 1953. The effect of X rays of different qualities on the alkaline phosphatase of living mouse bone. *British Journal of Radiology*, *26*, 38–46.

1981, *British Journal of Radiology*, *54*, 878–881

Total-body irradiation in advanced non-Hodgkin's lymphoma

By H. J. Dobbs, M.A., M.R.C.P., F.R.C.R., A. Barrett, M.B., B.S., F.R.C.R., *A. Y. Rostom, M.B., Ch.B., F.R.C.R. and M. J. Peckham, M.D., F.R.C.P.(G), F.R.C.R.

The Institute of Cancer Research, and the Royal Marsden Hospital, Downs Road, Sutton, Surrey

(*Received February 1981*)

Abstract

Thirty-seven patients with advanced non-Hodgkin's lymphoma who were treated by total-body irradiation (TBI) at the Royal Marsden Hospital are reviewed. Twenty-four patients had received no previous therapy; 13 patients were in relapse. The overall response rate was 73% for nodular lymphomas and 80% for those with diffuse disease. The duration of complete response ranged from two to 41 months (median 12 months). Subsequent chemotherapy was given successfully except in patients with prolonged thrombocytopenia which appeared to be related to an initially involved bone marrow. Hemibody irradiation (HBI) was the least myelosuppressive form of TBI and is now being used in complete remission following chemotherapy.

The majority of patients with non-Hodgkin's lymphoma (NHL) have disseminated disease at presentation and systemic therapy is therefore the most logical approach to their management. Single-agent chemotherapy regimes are relatively ineffective and more aggressive combination schedules have had only limited success.

Total-body irradiation has been used in the management of advanced lymphomas for over a decade. Johnson (1972) reported a series of 27 patients who received TBI and had a complete remission rate of 93% with a median remission duration of 26 months. It was hoped that these high complete remission rates might be reflected in increased survival when long-term follow-up became available. In 1978 a randomized trial of combination chemotherapy with cyclophosphamide, vincristine and prednisolone compared with TBI for advanced poorly-differentiated lymphomas was carried out by the National Cancer Institute (NCI) (Young *et al.*, 1977; Johnson *et al.*, 1978). They have studied 72 patients in all and found that response and survival rates are similar in the two groups.

This paper reports the experience of the Royal Marsden Hospital between 1973 and 1977 with TBI in the treatment of 37 patients with advanced lymphomas.

Methods and Materials

Thirty-seven patients were treated, of whom 24 had received no previous therapy. The remaining 13 patients were in relapse after previous chemotherapy or local radiotherapy. The median age was 56 years (range 25–82 years). All patients were investigated with chest radiography, lymphangiogram and intravenous urogram, bone marrow aspirate and trephine and liver function tests. Twelve patients had Stage III disease and 25 had Stage IV disease, using the Ann Arbor staging system.

All patients had proven histology classified according to Rappaport. Twenty-two patients had nodular lymphomas, and 15 patients had diffuse histology. Patients with diffuse histiocytic lymphomas were excluded. The distribution of patients according to histology is shown in Table I. No therapy was instituted in cases of nodular lymphoma until there was definite evidence of progressive disease.

Using a 6 MeV photon beam patients were irradiated in the sitting position with their arms crossed in front of the chest and tissue-equivalent material used as bolus between the legs. No part of the body was shielded. Doses were checked in all patients using lithium fluoride thermoluminescent dosimetry. Both sides of the body were treated at each session using two lateral fields. For low-dose TBI three treatment regimes were employed as outlined in Table II. When hemibody irradiation (HBI) was given, the most involved half was irradiated first and no skin gaps were left. Allopurinol was given to prevent uric acid uropathy.

TABLE I

Distribution of histology

	Nodular	Diffuse
MDLL	8	3
PDLL	10	3
WDLL	0	7
Mixed L-H	4	0
DU	0	2
Total	22	15

MDLL = moderately differentiated lymphocytic lymphoma.
PDLL = poorly differentiated lymphocytic lymphoma.
WDLL = well differentiated lymphocytic lymphoma.
Mixed L-H = mixed lymphocytic-histiocytic lymphoma.
DU = diffuse undifferentiated.

---

*Present address: Regional Radiotherapy Centre, St. Luke's Hospital, Warren Road, Guildford, Surrey.

Full blood counts were taken before each treatment and treatment was witheld if there was a rapid fall in platelet count.

RESULTS

The criterion for complete response was disappearance of all palpable and radiological disease. Partial response was defined as clearance of more than 50% of demonstrable disease for a period of three months. The complete response rate in patients with nodular disease was 64% (14 out of 22) with seven out of ten with poorly differentiated nodular lymphocytic lymphoma showing a complete response. In the diffuse group, 40% (six out of 15) showed a complete response (Table III). The overall response rate was 73% (16 out of 22) for the nodular lymphomas and 80% (12 out of 15) for the diffuse group. This overall response rate proved to be similar to that found at other centres as seen in Table IV (Choi *et al.*, 1979; Rees *et al.*, 1980; Thar *et al.*, 1979; Young *et al.*, 1977).

TABLE II

TOTAL BODY IRRADIATION PROTOCOLS

1 TBI	1.5 Gy mpd in 10 f and 12 days	13 patients
2 Protracted TBI (PTBI)	1.5 Gy mpd in 10 f twice weekly 5 weeks	13 patients
3 Hemibody irradiation (HBI)	3 Gy mpd in 10 f and 12 days. Other half 6–8 weeks later	11 patients

Note. mpd means mid-plane dose; f means fractions.

TABLE III

RESPONSE TO TBI

Histology	CR	PR	None	Total no. of patients
Nodular				
MDLN	4	2	2	8
PDLN	7	0	3	10
Mixed L-H	3	0	1	4
Total	14 (64%)	2 (9%)	6 (27%)	22
Diffuse				
MDLD	2	0	1	3
PDLD	2	1	0	3
WDLL	2	4	1	7
DU	0	1	1	2
Total	6 (40%)	6 (40%)	3 (20%)	15

Duration of response was measured from completion of TBI to the first objective evidence of relapse. The longest median duration of response was 26 months in a group with poorly differentiated nodular lymphocytic lymphoma. The range of duration of response was four to 41 months for nodular lymphomas and two to 36 months for diffuse tumours. The median duration of response for the whole group was 12 months.

Twenty-four patients had not received any other form of therapy before TBI and were analysed separately. For the patients with nodular lymphoma the response rate was ten out of 13 for those with no prior treatment compared with six out of nine for those who had been previously treated. The duration of response was 15 months in the previously untreated group compared with 12 months in those who had received prior treatment. We also compared those who had a complete response with those who had a partial response to see if complete remission led to an advantage in terms of longer disease-free interval. Those with a complete response had a disease-free interval of 11 months compared with 12 months to progression of disease for those who had a partial response.

Figure 1 shows a comparison between the survival in the nodular versus diffuse histology patients, with the median survival rates being 50 versus 42 months respectively. There was no difference in the actuarial survival rate of complete responders compared with partial or non-responders (Fig. 2).

Treatment was well tolerated and was given on an outpatient basis. Bone-marrow toxicity was the major complication with the lowest white-cell and platelet counts occuring at four to five weeks after completion of treatment. Fourteen out of 37 (38%) patients had marked thrombocytopenia with platelet counts of less than 50000/mm^3 but there were no serious bleeding problems. In six patients, no further chemotherapy was possible due to prolonged thrombocytopenia. Three of these patients had poorly

TABLE IV

OVERALL RESPONSE RATE

Series	Nodular	Diffuse
Choi *et al.*	26/31 (84%)	7/8 (87%)
Rees *et al.*	12/16 (75%)	3/6 (50%)
Thar *et al.*	29/30 (97%)	17/18 (94%)
Young *et al.*	32/33 (97%)	12/16 (75%)
Royal Marsden Hospital	16/22 (73%)	12/15 (80%)

TABLE V

CHEMOTHERAPY AFTER TBI

Marrow status	No chemotherapy needed post TBI	Chemotherapy impossible	Chemotherapy given
Involved	4/19	6/19	9/19
Not Involved	6/18	0/18	12/18

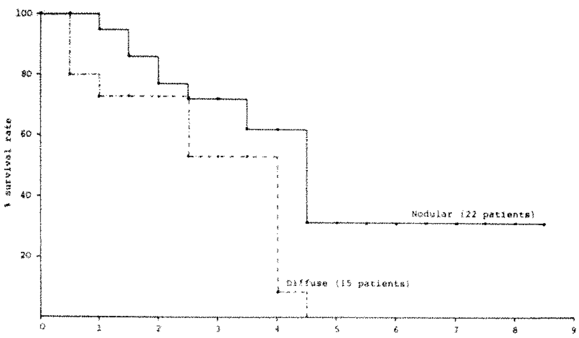


FIG. 1.

Nodular *vs.* diffuse lymphomas. Actuarial survival rates.

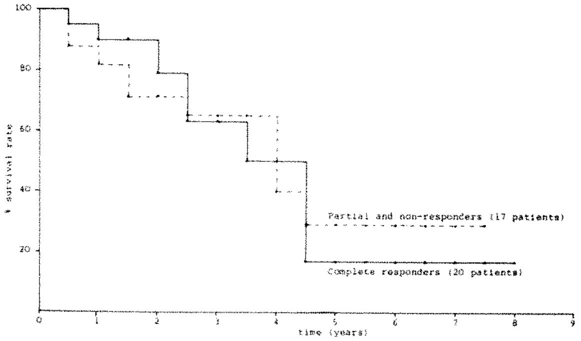


FIG. 2.

Complete *vs.* partial and non-responders. Actuarial survival rate.

differentiated nodular lymphocytic disease and three nodular mixed lymphoma. All six patients had an involved bone marrow. It is interesting to note that isolated thrombocytopenia also occurs after bone-marrow transplants (BMT) and autologous marrow grafts. This could theoretically be due either to there being no remaining normal stem cells following treatment, or persisting disease causing suppression of repopulation of the marrow, or damage to the bone marrow stroma.

Nineteen out of 37 patients had an involved bone marrow and six were unable to tolerate chemotherapy in relapse due to prolonged thrombocytopenia. The remaining 18 patients had a normal bone marrow and none of these were prevented from receiving further chemotherapy when they relapsed (Table V). Our earlier report that HBI is less myelosuppressive than TBI appears to be confirmed by this update. Five patients receiving HBI had a normal bone marrow and none of these developed prolonged thrombocytopenia, compared with two out of six patients with normal bone marrow who received TBI. The most significant factor appeared to be the presence of an involved bone marrow with five out of six in the HBI group and five out of seven receiving TBI developing marked thrombocytopenia.

Two out of 37 patients developed clinical hypothyroidism, one at seven months and the other at 50 months post-TBI. This is in comparison with nine out of 36 patients after mantle-field irradiation for Hodgkin's disease at this hospital at six months to 14 years (unpublished data). It is possible that these cases of hypothyroidism following TBI were radiation-induced but it could equally be a naturally occurring phenomenon in an elderly group of patients. No cases of hypothyroidism have been reported yet after high-dose single fraction TBI.

DISCUSSION

Our result of an overall response rate of 76% is in agreement with the reports of other authors on the efficacy of TBI in advanced NHL (Chaffey *et al.*, 1976). The response rate is similar to that reported with chemotherapy and is without serious toxicity. Subsequent chemotherapy was given successfully except in those patients with prolonged thrombocytopenia. However, one must conclude that TBI does not confer any advantage in terms of cure even in the complete responders. Haefliger *et al.* (1979) reported on changes in lymph-node size following systemic irradiation for advanced lymphomas in some of the patients presented here. Their conclusion that HBI produced a greater growth delay than

TABLE VI

Comparison of three TBI protocols

	Response	Complete remission	Median duration of response (months)
HBI	7/11 (64%)	7/11 (64%)	16
PTBI	11/13 (84%)	5/13 (38%)	14
TBI	9/13 (69%)	7/13 (54%)	10

TBI may be reflected in the greater median duration of response for patients receiving HBI as reported in this series (Table VI).

We are therefore currently studying the effect of giving chemotherapy first to obtain complete remission followed by sequential HBI to try and improve disease control and survival rate.

REFERENCES

Chaffey, J. T., Rosenthal, D. S., Moloney, W. C. and Hellman, S., 1976. Total body irradiation as treatment for lymphosarcoma. *International Journal of Radiation Oncology Biology Physics, 1*, 399–405.

Choi, N. C., Timothy, A. R., Kaufman, S. D., Carey, R. W. and Aisenberg, A. C., 1979. Low dose fractionated whole body irradiation in the treatment of advanced non-Hodgkin's lymphoma. *Cancer, 43*, 1636–1642.

Haefliger, J. M., Peckham, M. J. and Steel, G. G., 1979. Changes in lymph node size following systemic irradiation for malignant lymphoma. *Clinical Radiology, 30*, 5–10.

Johnson, R. E., 1972. Remission induction and remission duration with primary radiotherapy in advanced lymphosarcoma. *Cancer, 29*, 1473–1476.

Johnson, R. E., Canellos, G. P., Young, R. C., Chabner, B. A. and De Vita, V. T., 1978. Chemotherapy (cyclophosphamide, vincristine and prednisone) versus radiotherapy (total body irradiation) for Stage III–IV poorly differentiated lymphocytic lymphoma. *Cancer Treatment Reports, 62* (3), 321–325.

Rees, G. J. G., Bullimore, J. A., Lever, J. V. and Pizey, N. C. D., 1980. Total body irradiation as a secondary therapy in non-Hodgkin's lymphoma. *Clinical Radiology, 31*, 437–439.

Thar, T. L., Million, R. R. and Noyes, W. D., 1979. Total body irradiation in non-Hodgkin's lymphoma. *International Journal of Radiation Oncology Biology Physics, 5*, 171–176.

Young, R. C., Johnson, R. E., Canellos, G. P., Chabner, B. A., Brereton, H. D., Berard, C. W. and De Vita, V. T., 1977. Advanced lymphocytic lymphoma: randomized comparisons of chemotherapy and radiotherapy, alone or in combination. *Cancer Treatment Reports, 61* (6), 1153–1159.

Book reviews

Lecture Notes on Clinical Oncology. By Barry W. Hancock and J. David Bradshaw, pp. vii+215, 1981 (Blackwell Scientific Publications, Oxford), £5.50.
ISBN0-632-00674-9

Those senior members of the profession who are usually asked to review books in the columns of august journals in this country tend to sneer at students' handbooks. They often take delight in detailing the omission of sections which they claim to be essential reading. It is possible to provide a readable, accurate and up-to-date account of the aetiology, investigation and management of cancer, subdivided both by organ of origin and treatment modality, and compress it into 200 pages of a small pocket book. I believe that Drs. Hancock and Bradshaw have done this successfully and I congratulate them. It is a much more difficult task than compiling a large monograph on a single aspect of cancer.

This is not a cram book for students. It is background reading intended to provide a balanced viewpoint of the team approach to cancer. It is directed to undergraduate and postgraduate students, but in my opinion it could usefully be dipped into, as the occasion demands, by those nurses, radiographers, physicists and social workers who are associated with the management of the cancer patient. It is free from those technical and histopathological photographs which tend to put off the non-specialist student. It even has sections on cancer education, screening, prevention and terminal care.

By its very nature, the approach of the book must be broad and superficial. How else, for example, can you cover the subject of breast cancer in eight small pages, including its aetiology, epidemiology, pathology, clinical presentation and staging, diagnosis, hormone receptor assay, management by surgery, radiotherapy, endocrine and chemotherapy, prognosis and screening? There are a few spelling mistakes and errors in syntax. These are small criticisms of a book which aims to present a consensus in a subject which is in a constant state of flux and where the members of the management team may have differing views on the efficacy of the modalities employed in treatment.

Basil A. Stoll.

Roentgenology of Lymphomas and Leukemias. By Benjamin Felson, pp. x+134, 1980 (Grune and Stratton, New York), $24.50.
ISBN 0-8089-1333-6

Twenty separate authors have contributed to this book under the editorship of Dr. Benjamin Felson.

The separate chapters on diagnostic radiology are preceded by chapters on pathology, staging and management, and variants and pre-lymphomatous disorders. These are lucid, comprehensive and make an excellent introduction to the radiology.

The chapters on radiology are of a uniformly high standard, and how refreshing it is to find a series of authoritative contributions giving facts and figures, indications of when to use the various techniques and, even more important, when not to use them. The logic behind their recommendations is clearly set out.

The figures in themselves are interesting. For instance, the incidence of disease in the thorax for both Hodgkin's Disease and non-Hodgkin lymphoma is about double the incidence we have found in London, whereas below the diaphragm they are much the same. One feels that in Chapter 3 there should have been a section on Mediterranean lymphoma although this is mentioned in Chapter 6, because this fits so well into the grey zone which was being discussed. This, however, is a very small point.

I found this a very readable book, written by experts, clearly set out, authoritative, well illustrated and I would unhesitatingly recommend it.

J. S. Macdonald.

1981, *British Journal of Radiology*, *54*, 882–898

European protocol for neutron dosimetry for external beam therapy

By J. J. Broerse, B. J. Mijnheer and J. R. Williams

European Clinical Neutron Dosimetry Group (ECNEU)

(*Received October 1980 and in revised form April 1981*)

Contents

1. Introduction
2. Principles of dosimetry of neutron fields
3. Dosimetric methods
    3.1. Ionization chambers
    3.2. Materials
4. Physical parameters
    4.1. Average energy required to create an ion pair, W_N
    4.2. Gas-to-wall absorbed dose conversion factor, $(r_{m,g})_N$
    4.3. Neutron kerma ratio, $(K_t/K_m)_N$
    4.4. Displacement factor, $(k_d)_T$
    4.5. Relative neutron sensitivity, k_U
5. Determination of absorbed dose at a reference point
    5.1. Gamma-ray calibration
    5.2. Neutron absorbed-dose measurement
6. Determination of absorbed dose at any point
    6.1. Central-axis absorbed-dose distribution
    6.2. Isodose distributions
    6.3. Absorbed-dose specification
    6.4. Description of irradiation technique
7. Check of absorbed dose given to a patient
    7.1. Absorbed-dose monitoring systems
    7.2. *In vivo* dosimetry
8. Dosimetry intercomparisons between institutes
    References
    Appendix I: List of symbols
    Appendix II: Code of practice

1. INTRODUCTION

A common basis for neutron dosimetry will be one of the essential requirements for the comparison of clinical results obtained at the increasing number of fast-neutron radiotherapy facilities. Co-operation between the physicists involved in fast-neutron radiotherapy has been established in Europe by the High LET Therapy Project Group under the sponsorship of the European Organization for Research on Treatment of Cancer, EORTC. In September 1978, the clinical group decided that the physicists should intensify their contacts and organize a formal co-operation. For this purpose a European Clinical Neutron Dosimetry Group, abbreviation ECNEU, was established. In the United States all groups involved in or planning fast neutron therapy have directly or indirectly participated in the Fast Neutron Beam Dosimetry Physics Task Group 18 of the Radiation Therapy Committee of the American Association of Physicists in Medicine (AAPM).

Protocols for neutron dosimetry for radiotherapy have been drafted for the European (Broerse and Mijnheer, 1976) and the American groups (Eenmaa and Wootton, 1978). The main items of the two drafts were recently summarized by Broerse *et al.* (1979). Both groups, ECNEU and Task Group 18, have introduced a number of improvements which resulted in the final draft of the American protocol (AAPM, 1980) and the present contribution.

Both protocols quote ICRU Report 26 (1977) as the main source of information on methodology and basic physical data for neutron dosimetry. It should be emphasized that efforts are continuing to improve the data base of neutron dosimetry. For some physical parameters the present protocol will therefore give recommended values which differ from the ones quoted in ICRU Report 26 and may be subject to changes in the future. They can, however, be used as a common basis for clinical neutron dosimetry, if accepted by all fast-neutron therapy centres. Two international neutron dosimetry intercomparisons, INDI (ICRU, 1978a) and ENDIP (Broerse *et al.*, 1978), have been performed. Both yielded the same conclusions, namely that to reduce systematic dosimetry differences it will be necessary to standardize on the basic physical parameters and on the experimental instruments and techniques employed.

The present European protocol has been developed in parallel with the US protocol. The differences in dosimetry procedures between the European and American groups will be indicated if

---

The final draft of this protocol was based upon discussions with a number of ECNEU members. The current membership of ECNEU is:
J. J. Broerse, Rijswijk, The Netherlands (Chairman);
B. J. Mijnheer, Amsterdam, The Netherlands (Secretary);

G. Burger, Neuherberg, FRG;
E. Byrski, Krakow, Poland;
D. Greene, Manchester, UK;
A. Hess, Hamburg, FRG;
K. H. Höver, Heidelberg, FRG;
J. P. Meulders, Louvain, Belgium;
C. J. Parnell, London, UK;
J. Rassow, Essen, FRG;
K. Regel, Rossendorf, GDR;
M. Salzmann, Villigen, Switzerland;
W. Seelentag, Zürich, Switzerland;
R. Strang, Glasgow, UK;
J. R. Williams, Edinburgh, UK.

Requests for reprints should be sent to B. J. Mijnheer, Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.

relevant. The present document is intended to serve the immediate needs of participating European centres and should contribute to improved accuracy and reproducibility of fast neutron dosimetry.

2. PRINCIPLES OF DOSIMETRY IN NEUTRON FIELDS

Neutron fields are always accompanied by γ rays originating from the neutron-producing target, from the primary shielding and field-limiting system, and from the biological object or phantom being irradiated. Because of the differences in relative biological effectiveness of these two radiation components (which may depend on the specific biological end-point), it is necessary to determine separately the neutron absorbed dose in tissue, D_N, as well as the γ-ray absorbed dose in tissue, D_G. To compare the biological and clinical effects of neutron beams of different energies, it will be important to obtain information about the radiation quality which can be related to neutron energy spectra or microdosimetric spectra (see, *e.g.*, ICRU 1977; Booz, 1979; Broerse and Mijnheer, 1981). This aspect will not be treated in this protocol.

An evaluation of the separate absorbed dose components can be made with a single instrument such as a proportional counter. This method requires the unfolding of the energy deposition events caused by protons and heavy ions from those caused by electrons (Caswell, 1960; Weaver *et al.*, 1977; August *et al.*, 1978). Generally, however, two instruments with different relative neutron sensitivities are used for the evaluation of the component radiations. One of these, *e.g.* a tissue-equivalent (TE) ion chamber or a TE calorimeter, will have approximately the same sensitivity to neutrons and photons, whereas the second instrument is chosen for its reduced neutron sensitivity relative to that for photons.

The absorbed dose components in the mixed field can be computed by the use of the following simultaneous equations:

$$R_T' = k_T D_N + h_T D_G \quad . \quad . \quad . \quad (2\text{–}1)$$

$$R_U' = k_U D_N + h_U D_G \quad . \quad . \quad . \quad (2\text{–}2)$$

In these equations the subscript T refers to the tissue-equivalent device measuring total absorbed dose and the subscript U refers to the neutron insensitive device. R_T' and R_U' are the quotients of the readings of the two dosemeters in the same mixed beam relative to their sensitivities to the γ rays used for the photon calibration. Similarly, k_T and k_U are the sensitivities of each dosemeter to neutrons relative to its sensitivity to the γ rays used for calibration, and h_T and h_U are the sensitivities of each dosemeter to the photons in the mixed field relative to its sensitivity to the γ rays used for calibration. A more detailed definition of k_T and h_T is given in Section 3.1. The values of h_U and h_U are close to unity and the simplifying assumption $h_T = h_U = 1$ is usually made. The numerical values of k_T and k_U for specific devices will be discussed in Section 4.

3. DOSIMETRIC METHODS

The use of calibrated A-150 plastic TE ionization chambers with TE gas filling is recommended as the practical method of obtaining the tissue kerma in air and the absorbed dose in a TE phantom. This recommendation is based on the fact that TE chambers have been used as the principal dose measuring instrument by the neutron therapy groups in Europe, USA and Japan which are currently regularly treating patients. The American groups all use a common set of TE ionization chambers. Typically, they employ a 1.0 cm^3 spherical chamber as the principal instrument for measurements of neutron tissue kerma in air and absorbed dose in a phantom, and a 0.1 cm^3 cylindrical chamber for spatial dose distribution measurements in a TE liquid phantom. In Europe, the institutes developed and constructed their own dosemeters; these, unavoidably, show mutually different characteristics. It has been decided that all European groups should also use a common type of ionization chamber to check their other dosemeters. For specific information on technical characteristics the reader is referred to the Monograph on Ion Chambers for Neutron Dosimetry (Broerse, 1980).

The TE ionization chambers should have applied to them a calibration factor for ^{60}Co, ^{137}Cs or 2 MV X rays. This calibration should be directly traceable to a national standards laboratory. The ionization chamber method can be compared with other measurement systems, and in particular those that do not require calibration in a known radiation field are useful. A dosemeter which can be used for this purpose is the TE calorimeter (McDonald *et al.*, 1976; ICRU, 1977). An alternative method for the determination of neutron kerma is to measure fluence and apply a fluence to kerma conversion factor. Activation detectors and fission counters (Porter *et al.*, 1975) can be used for this purpose.

3.1. *Ionization chambers*

The absorbed dose, D_g, in the gas cavity of an ionization chamber is given by:

$$D_g = \underset{\sim}{Q}\frac{W}{e}\frac{1}{m} \quad . \quad . \quad . \quad . \quad (3.1\text{–}1)$$

where Q is the total charge produced within the cavity, W is the average energy required to produce an ion pair in the gas, e is the charge of the electron and m is the mass of gas within the cavity.

In the SI-system D_g is expressed in Gy, Q in C, W in J, e in C and m in kg. Absorbed dose in the wall material adjacent to the cavity of the chamber, $D_m{}^*$, can be calculated from the energy absorbed by the gas using the gas-to-wall absorbed-dose conversion factor, $r_{m,g}$, similar to r introduced by Bichsel and Rubach (1978).

$$D_m{}^* = r_{m,g} D_g \quad . \quad . \quad . \quad (3.1\text{–}2)$$

If the charged particles produced within the wall of the chamber lose a negligible part of their energy in crossing the cavity, then the conditions for the Bragg-Gray theory are satisfied and r is identical to $s_{m,g}$, the ratio of the mass stopping powers in the wall to the gas of the particles produced in the wall of the chamber. For photon radiation this charged particle fluence will consist of electrons, while for neutrons it will, in general, consist of electrons, protons, helium nuclei, and heavy recoils such as carbon, oxygen and nitrogen nuclei (Caswell and Coyne, 1972). For a cavity whose size is not negligible in relation to the range of the secondary charged particles generated in the wall, it is necessary to make more detailed calculations for the values of r as a function of cavity size and neutron energy.

If the chamber wall is replaced by reference tissue, the absorbed dose in the tissue adjacent to the cavity of the chamber, $D_t{}^*$, is calculated from $D_m{}^*$ using the ratio of mass energy absorption coefficients, $(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_m$, in the tissue and wall material, assuming that there is charged particle equilibrium:

$$D_t{}^* = \frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_m} D_m{}^* \quad . \quad . \quad (3.1\text{–}3)$$

Combining these equations one obtains:

$$D_t{}^* = \frac{Q}{m}\frac{W}{e} r_{m,g} \frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_m} \quad . \quad . \quad (3.1\text{–}4)$$

For measurements with an ionization chamber the reading obtained from the chamber, R, has to be related to the charge produced within the cavity at a reference temperature and pressure by the product of several correction factors, Πk_R:

$$Q = R \Pi k_R \quad . \quad . \quad . \quad . \quad (3.1\text{–}5)$$

The factors contained in Πk_R include the electrometer calibration factor and correction factors for ion recombination, temperature and pressure, gas flow rate and leakage current, and will be discussed in more detail in Sections 5.1 and 5.2.

To apply equation (3.1–4) the mass of gas in the cavity has to be known. This can be obtained from the calibration factor of the tissue-equivalent chamber with photons, α_c, which is defined as:

$$\alpha_c = \frac{(D_t{}^*)_c}{Q_c} \quad . \quad . \quad . \quad . \quad (3.1\text{–}6)$$

where subscript c refers to the photon calibration beam. If this is substituted into equation (3.1–4) we obtain:

$$m = \frac{1}{\alpha_c}\frac{W_c}{e}(s_{m,g})_c \left[\frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_m}\right]_c \quad . \quad (3.1\text{–}7)$$

In this equation the gas-to-wall absorbed dose conversion factor, $r_{m,g}$, has been replaced by $(s_{m,g})_c$ since the chambers used for clinical neutron dosimetry are usually small enough to satisfy the conditions for the Bragg-Gray theory at the photon calibration energies normally used. The measurement of the calibration factor, α_c, will be discussed in Section 5.1.

It is now possible to use equation (3.1–4) to calculate the absorbed dose in tissue in a neutron beam. However, neutron beams used for radiotherapy include a photon component which contributes to the total absorbed dose, and equation (3.1–4) has to be modified to express the total charge collected, Q_T, in terms of the separate neutron and photon components of absorbed dose (D_N and D_G). In addition it must be remembered that equation (3.1–4) gives the absorbed dose in the wall material adjacent to the cavity of the ionization chamber, whereas for clinical dosimetry measurements in a phantom the required result is the absorbed dose at the position of the centre of the chamber when the chamber is replaced by the phantom material. Therefore a displacement factor $(k_d)_T$ is introduced which corrects for the lack of attenuation and scattering in the cavity of the chamber. $(k_d)_T$ is the ratio of D_g for an infinitesimally small cavity to that which is measured. Equations (3.1–4), (3.1–5) and (3.1–7) can then be used to relate the measured charge to the two separate absorbed-dose components:

$$R_T(\Pi k_R)_T(k_d)_T\alpha_c = k_T D_N + h_T D_G \quad (3.1\text{–}8)$$

where $k_T = \dfrac{W_c}{W_N}\dfrac{(s_{m,g})_c}{(r_{m,g})_N}\dfrac{[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_m]_c}{(K_t/K_m)_N}$

$$h_T = \frac{W_c}{W_G}\frac{(s_{m,g})_c}{(s_{m,g})_G}\frac{[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_m]_c}{[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_m]_G}$$

and subscripts N and G refer to the neutron and photon components respectively. It has been assumed that the displacement factor for the separate absorbed dose components cannot readily be evaluated. It is therefore more appropriate to apply it to the total ionization.

It should be noted that in the equation for k_T the ratio of the mass energy absorption coefficients for neutrons has been replaced by the ratio of kerma in tissue and in wall material $(K_t/K_m)_N$. The physical parameters to go into k_T will be discussed in more detail in Section 4.

The product $R_T(\Pi k_R)_T a_c$ is identical to R_T' as defined in equation (2.7–1) in ICRU Report 26. The neutron and photon doses in the ICRU equation are at the effective centre of the chamber, whereas equation (3.1–8) gives D_N and D_G at the position of the geometrical centre of the chamber when it is replaced by phantom material.

The reading of a TE ionization chamber in a neutron beam is sometimes interpreted as being proportional to the total absorbed dose, D_N+D_G. The validity of this approximation can be assessed by rewriting equation (3.1–8) as:

$$R_T(\Pi k_R)_T(k_d)_T a_c = k_T(D_N+D_G)(1+\delta) \quad . \quad . \quad . \quad . \quad (3.1\text{–}9)$$

where $\delta = \dfrac{D_G}{D_N+D_G}\,\dfrac{h_T-k_T}{k_T}$.

It is usual to assume that h_T is unity and generally k_T lies in the range 0.95–1.00. For radiotherapy beams D_G is generally less than 20% of the total absorbed dose within the main beam, so that δ is usually less than 0.01. Therefore, if equation (3.1–9) is used with a zero value for δ, the error introduced into the calculation of D_N+D_G is usually less than 1%. The approximation that the parameters appropriate to neutrons only can be applied for the mixed beam has been adopted by the neutron therapy groups in the US.

3.2. *Materials*

A common electrically conductive plastic used in the construction of TE ionization chambers has been a particular muscle-equivalent formulation designated A-150.*

A-150 plastic is generally supplied as small chips or granules suitable for use in moulding, or in various sizes of stock and custom-moulded shapes for more direct use. It consists of a homogeneous mixture of polyethylene, nylon (Du Pont Zytel 69), carbon and calcium fluoride (Smathers *et al.*, 1977).

TABLE 3–1.
ELEMENTAL COMPOSITION BY WEIGHT OF A-150 MUSCLE-EQUIVALENT PLASTIC, MUSCLE-EQUIVALENT GAS AND ICRU MUSCLE TISSUE

Element	ICRU muscle*	A-150 plastic†	TE-gas‡
H	10.2	10.2±0.1	10.2
C	12.3	76.8±0.5	45.6
O	72.9	5.9±0.2	40.7
N	3.5	3.6±0.2	3.5
Ca	0.007	1.8±0.1	—
F	not listed	1.7±0.1	—
Others	1.1	—	—

*ICRU (1964).
†Smathers *et al.* (1977).
‡Rossi and Failla (1956), % partial pressure: 64.4% CH_4, 32.4% CO_2, 3.2% N_2.

Based on extensive experimental and computational analysis of the end product, Smathers *et al.* have arrived at the elemental weight composition for A-150 plastic given in Table 3–1 (see also Goodman 1978). Ideally, each new batch of mixture which is intended for fabrication of instrument components for which the elemental composition is critical should be analyzed thoroughly either at its source or by the user. In particular, the user should be aware that the accuracy of the measured neutron dose is very strongly dependent on the exact hydrogen content of the material.

A-150 TE plastic is not identical in elemental composition to ICRU muscle tissue due to the large admixture of carbon required for electrical conductivity (Table 3–1). Deviations from muscle equivalence will thus necessarily be reflected in a kerma-factor ratio for the two media which is different from unity.

The density of moulded A-150 plastic is 1.127 ±0.005 g/cm^3 and does not appear to depend on the moulding technique (Goodman, 1978).

Tissue-equivalent gas is recommended for use in homogeneous TE ionization chambers for measuring the total absorbed dose. The recommended formulation and composition of the TE gas are also given in Table 3–1. The composition of the gas should be verified by analysis since impurities in the gas may have a significant effect on the chamber response.

4. PHYSICAL PARAMETERS

Variation in the results obtained in neutron dosimetry intercomparisons can, in part, be traced to differences in the basic physical parameters which have been used to convert specific dosemeter reading to tissue kerma in free air or to absorbed dose in a phantom (Almond and Smathers, 1977; ICRU, 1978a; Broerse *et al.*, 1978). These parameters are:

---

*Supplied by Physical Sciences Laboratory, Illinois Benedictine College, Lisle, Illinois 60532, USA.

(1) the average energy required to create an ion pair in the gas, W_N;
(2) the gas-to-wall absorbed-dose conversion factor, $r_{m,g}$;
(3) the neutron kerma ratio, $(K_t/K_m)_N$;
(4) the displacement factor, $(k_d)_T$;
(5) the relative neutron sensitivity of dosemeters used for photon-fraction determinations, k_U.

In order to achieve consistency in neutron dosimetry, it will be necessary to use a set of these basic parameters which is appropriate for a given neutron spectrum and which is obtained from a common source.

Neutron spectral measurements are the necessary source input for computation of these basic physical parameters, These measurements have been accomplished by many methods, *e.g.* proton recoil counters, time-of-flight and foil activation. The techniques are those developed over a period of years for use in reactor and neutron physics research. For neutrons above 20 MeV, deficiencies in the cross-section information tend to increase the uncertainty in the data with increasing energy.

Some types of detectors, *e.g.* Geiger-Müller counters, have a sensitivity which varies with photon energy. In order to determine the relative photon sensitivity h_T or h_U of these dosemeters, an approximate knowledge of the photon spectrum in the neutron field is necessary. When no information is available, h_T and h_U are taken equal to unity. This may introduce an uncertainty of several per cent in the determination of the photon absorbed dose in a neutron beam.

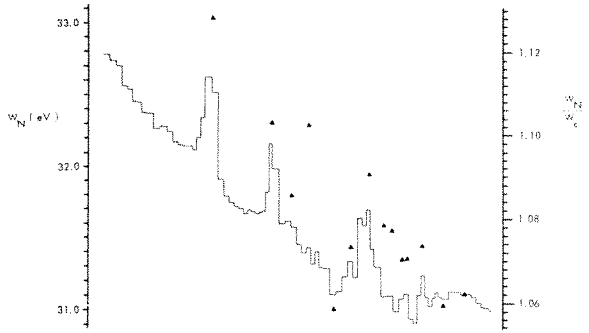


FIG. 4-1.

W_N values calculated for methane-based tissue equivalent gas by Goodman and Coyne (1980). The triangular points shown on the graph are values of W_N evaluated at point energies of prominent resonances, rather than the values averaged over energy bins shown by the solid lines.

4.1. *Energy required to create an ion pair, W_N*

The parameter which is used to convert the charge produced within the chamber to energy deposited in the gas is W, the mean energy required to form an ion pair in the chamber gas or gas mixture. The magnitude of this parameter depends on the type and spectra of the secondary charged particles, and on the chemical composition of the gas.

In the European as well as in the US institutions engaged in neutron therapy, values of W_c/W_N of 0.95 to 0.96 have been used for TE gas. ICRU (1977) recommended a value of 0.95, with an estimated uncertainty of about 5% for neutron energies higher than 1 MeV. Goodman and Coyne (1980) presented detailed calculations of W_N as a function of neutron energy, using more recent data on W values for charged particles in TE gas. The results of their calculations are shown in Fig. 4–1. It is recommended that the ratio of W_N/W_c be taken from this figure using the differential neutron fluence spectra multiplied by the tissue kerma factor. If no spectra are available a value of 1.06 can be taken for most radiotherapy beams. An uncertainty of ±4% in this ratio has been estimated by Goodman and Coyne (1980).

4.2. *Gas-to-wall absorbed dose conversion factor, $(r_{m,g})_N$*

The gas-to-wall dose conversion factors for neutrons have been compromised in their accuracy due to several basic problems: (a) adequate measurements of stopping power have not been made for the charged particles generated by fast neutrons in A-150 plastic or in TE gas; (b) the equilibrium charged-particle spectrum created by the neutrons is not well-known; (c) the range of the low-energy heavy recoils is limited. The latter results in particles existing in the various categories of "starters", "stoppers", "insiders" and "crossers" relative to the the chamber cavity (Caswell, 1966) and the dose conversion factor is therefore a function of cavity size and neutron energy.

Values presently used by the European and US neutron therapy groups can be found in Smith *et al.* (1975) and Broerse *et al.*, (1978). Bichsel and Rubach (1978) have calculated dose conversion factors for a TE plastic–TE gas ionization chamber which approximates a Bragg-Gray cavity and for chambers of finite volume, taking into account the ionization due to primary charged particles (protons, helium nuclei, and C, N and O nuclei) originating in the gas (*i.e.* starters and insiders), relative to the total ionization; they also accounted for the possible differences in the stopping powers for solids and gases. Their results for

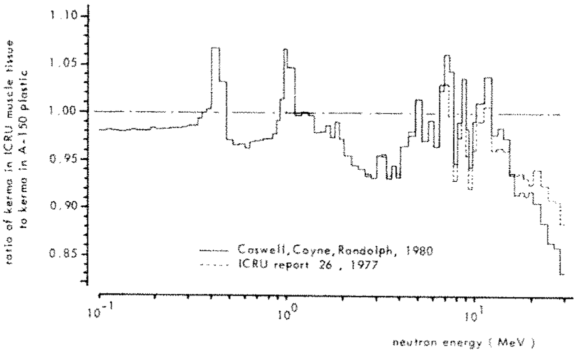


FIG. 4–2.

Ratio of kerma in ICRU muscle tissue to kerma in A-150 plastic based on the 1977 and 1980 kerma factors from Caswell *et al.*

a 2 cm^3 TE plastic–TE gas chamber vary between 0.987 and 0.993 for neutron energies between 5 and 14 MeV respectively. This indicates a value of $(r_{m,g})_N = 0.99$ for the neutron beams in current use. This new value would be about 1% lower than that used previously. It should be realized, however, that Bichsel and Rubach (1978) recommend an uncertainty of 4 to 5%.

A value of 0.99 ± 0.02 for $(r_{m,g})_N$ is recommended in combination with a value of 1.00 for $(s_{m,g})_c$. It should be noted that the product of the newly recommended W values and conversion factor $(r_{m,g})_N$ will not introduce large changes in the value of k_T based on the recommendations given in ICRU Report 26.

4.3. *Neutron kerma ratio*, $(K_t/K_m)_N$

The relevant quantity for medical and biological applications of fast neutrons is the absorbed dose in tissue of specific composition, *e.g.* soft tissue as defined by ICRU (1964) for muscle (Table 3–1). The differences in the oxygen and carbon content of TE plastic and muscle tissue and differences in the oxygen and carbon neutron cross sections will result in a muscle/TE plastic (A-150) kerma ratio which deviates from unity. A ratio in the range 0.93–0.97 has to be taken for the neutron therapy beams presently used for treating patients. The uncertainty associated with the ratio increases with neurton energy because of a lack of cross-section information in the higher energy range (ICRU, 1977).

Until now kerma ratios have usually been obtained from the tables of kerma per unit neutron fluence calculated by Caswell, Coyne and Randolph and published in ICRU Report 26 (ICRU, 1977). Recently, these authors (Caswell *et al.*, 1980) presented an updated version of their tables which show some changes from the earlier ones. These differences are particularly significant in oxygen between 7 and 13 MeV and in carbon above 15 MeV. Figure 4–2 compares $(K_t/K_m)_N$ calculated from these two sets of data. It is recommended that the more recent tables should be used for the calculation of kerma ratios. Uncertainties in the muscle/A-150 plastic kerma ratio increase with rising neutron energy and vary between 2.6% for a d(16)+Be spectrum to 9.7% for a p(66)+Be spectrum (Bewley, 1980).

Kerma calculations will obviously be spectrum dependent and attempts should be made to obtain information concerning the radiation spectrum at the reference point. Changes in neutron spectrum as the beam passes into a phantom or patient will probably not affect the kerma ratio much (Bewley, 1980).

4.4. *Displacement correction factor*, $(k_d)_T$

For absorbed dose specification as a function of depth and/or position in a large tissue-equivalent phantom, the analysis of dosimetric measurements using ionization chambers must account for the displacement of the phantom material brought about by the introduction of the dosemeter. A displacement correction is to be applied to the measured ionization charge (dose) to compensate for the differences in attenuation and scattering of the primary radiation caused by the displacement of the phantom material by the ion chamber, thus obtaining the charge (dose) which would have been measured by a hypothetical ion chamber of zero volume centered at the same location, for which the displacement correction factor would be unity.

This correction can be taken into account by using a multiplicative correction factor as measured by Shapiro *et al.* (1976). Another approach is to account for the displacement by stating the effective measuring point as a certain fraction of the radius of the gas cavity of the ionization chamber in front of the geometrical centre. The application of a multiplicative displacement correction factor is preferable at the reference point. The US protocol recommends two values for multiplicative displacement correction factors for their two common ionization chambers. In Europe where detectors of significantly different volume and shape are in use, the displacement correction factor measured by Zoetelief *et al.* (1980) for d+T neutrons should be used in equation (3.1–8) for the neutron-beam calibration at the reference point. This factor is given by $(k_d)_T = 1 - 2.5 \times 10^{-3} r_i$, where r_i is the radius of the cavity in millimetres. The uncertainties in the displacement correction factor (*e.g.* dependence on neutron energy) indicate the importance of using small ionization chambers.

4.5. *Relative neutron sensitivity*, k_U

Assessment of the photon component of absorbed dose in a neutron beam is made using a dosemeter which is relatively insensitive to neutrons. When used in conjunction with a dosemeter with approximately equal sensitivities to neutrons and photons, the separate absorbed dose components can be calculated by solving the simultaneous equations (2–1) and (2–2). The accuracy to which neutron absorbed dose can be calculated is greatest when a dosemeter with the smallest possible neutron sensitivity relative to its photon sensitivity, k_U, is used (ICRU, 1977). A dosemeter which has a particularly low k_U value is a small Geiger-Müller counter (*e.g.* Philips type 18529, Mullard type ZP1300) used with an energy compensating filter. Recent measurements of k_U for this detector have been made by several groups and the data are reviewed by Mijnheer *et al.* (1979). GM tubes with their energy compensating filters have a high thermal-neutron sensitivity and should be shielded by a thermal-neutron absorber which does not emit prompt γ radiation in the neutron capture process. A commonly chosen material is ^{6}Li in the form of the metal or ^{6}LiF powder. It should be noted that these detectors have a dead time of approximately 20 μs and at photon absorbed dose rates in excess of about 2 mGy min^{-1} the dead-time correction to be applied may be too high to permit accurate results. Also in high-intensity pulsed beams the dead time might cause difficulties. If it is not possible to reduce the output of the neutron source sufficiently, another type of dosemeter has to be used.

The most commonly used alternative dosemeter and that which is preferred by many of the US neutron therapy groups is the non-hydrogenous ionization chamber. Several wall and gas combinations have been used, in particular C–CO_2 and Mg–Ar. The former chamber has a higher k_U value, approximately 0.32 at 15 MeV, has different saturation characteristics to neutrons and photons (Maier and Burger, 1978), and also shows anomalous characteristics due to gas leakage through the graphite walls (Maier and Burger, 1978; Pearson *et al.*, 1980). Its use is therefore not recommended. Values of k_U for non-hydrogenous chambers have been measured by several authors, *e.g.* Ito (1978) and Waterman *et al.* (1979). The latter report shows that the variation of k_U with neutron energy is most marked in the range 7 to 15 MeV which covers a wide range of neutron source spectra currently being used for radiotherapy. It should be recognized that measurements of k_U made in air cannot be applied to determine the photon dose component in phantom unless the walls of the chamber are thick enough to stop the most energetic recoil protons generated in the phantom. The values given in Table 4–1 for a C–CO_2 chamber, an Al–Ar chamber and a GM counter are recommended for use as a guideline only. It should be emphasized that k_U varies with cavity size so that any measured data are only valid for the specific geometry of the chamber being used (Makarewicz and Pszona, 1978; Mijnheer, 1980).

5. Determination of Absorbed Dose at a Reference Point

5.1. *Gamma-ray calibration*

Determination of the calibration factor with photons, a_c, as defined in equation (3.1–6), is usually made with an exposure standard chamber whose calibration is directly traceable to a national standards laboratory. The calibration should be made in air with the geometrical centre of the detectors being

TABLE 4–1

Relative neutron sensitivities and their overall uncertainties for non-hydrogenous ionization chambers* and GM counter

Neutron energy (MeV)	Per cent energy spread	Relative neutron sensitivity, k_U			
		C–CO_2 chamber		A1-Ar chamber	GM counter
		Computed	Observed	Observed	
0.7	25	0.05	0.07 ± 0.006	0.014 ± 0.004	—
2	5	0.07	0.08 ± 0.01	0.012 ± 0.002	0.005†
5	6	0.07	0.11 ± 0.01	0.011 ± 0.003	0.007†
15	7	0.31	0.32 ± 0.02	0.13 ± 0.01	0.017†
252Cf	Fission spectrum	0.08	—	0.02 ± 0.015	—
d(16) + Be	Broad spectrum	—	0.150‡	0.061‡	$0.0073 + 0.0007$‖
d(50) + Be	Broad spectrum	—	0.405‡	0.219‡	—

*ICRU (1977).
†Mijnheer *et al.* (1979).
‡Ito (1978) for C-CO_2 chamber and Mg-Ar chamber.
‖Hough (1979).

taken as the point of measurement. A build-up cap of the same material as the wall should be added if the wall thickness of the TE chamber wall is not sufficient to achieve charged-particle equilibrium. The chamber should be orientated so that its stem is perpendicular to the beam.

Absorbed dose in TE plastic adjacent to the cavity of the TE chamber can be calculated (Mijnheer and Williams, 1981) from the measured exposure, X_c:

$$(D_{TE}^*)_c = X_c \frac{(W_{air})_c}{e}\left[\frac{(\mu_{en}/\rho)_{TE}}{(\mu_{en}/\rho)_{air}}\right]_c (\Pi k_A)_c. \qquad (5.1\text{–}1)$$

The correction factor $(\Pi k_A)_c$, which will be discussed in more detail later, accounts for the attenuation and scattering by the wall, central electrode and build-up cap of the chamber and also for the radiation scattered by the stem of the chamber into the sensitive part of the chamber. In addition corrections should be made if there is any radial or axial non-uniformity in the field, that is in the plane perpendicular to the central axis of the beam or along the central axis.

Absorbed dose in tissue is calculated from absorbed dose in TE plastic by

$$(D_t^*)_c = (D_{TE}^*)_c\left[\frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_{TE}}\right]_c$$

yielding

$$(D_t^*)_c = X_c (f_t)_c (\Pi k_A)_c \quad . \quad . \ (5.1\text{–}2)$$

where:

$$(f_t)_c = \frac{(W_{air})_c}{e}\left[\frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_{air}}\right]_c$$

The calibration factor with photons can now be rewritten as:

$$a_c = \frac{X_c (f_t)_c (\Pi k_A)_c}{R_c (\Pi k_R)_c} = N_c (f_t)_c (\Pi k_A)_c \ (5.1\text{–}3)$$

It should be noted that the product $X_c (f_t)_c (\Pi k_A)_c$ does not represent the absorbed dose in tissue in the absence of the chamber but it represents the absorbed dose in tissue adjacent to the cavity of the chamber. N_c is the exposure calibration factor, defined as:

$$N_c = \frac{X_c}{R_c (\Pi k_R)_c}$$

It is recommended that a value for $(f_t)_c$ (ICRU muscle) of 9.63×10^{-3} Gy/R is adopted in calculating the absorbed dose from exposure in ^{60}Co photon beams. $(f_t)_c$ can be calculated with $(W_{air})_c/e = 33.85$ J/C (ICRU, 1979) and $[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_{air}]_c = 1.103$ (Hubbell, 1977). It is assumed that N_c is supplied in R divided by the meter reading in C or divisions. If exposure is given in C kg^{-1}, the value of $(f_t)_c$ should be divided by 2.58×10^{-4}.

The correction factors, $\Pi k_R = k_e k_{t,p} k_s k_l k_p k_f k_h$, which convert the reading, R, taken from the chamber, to the charge, Q, produced within an ideal cavity at a reference temperature and pressure, will now be discussed in detail.

k_e: *Electrometer calibration factor.* This factor relates the reading of the electrometer to the actual charge measured. It is not necessary to measure the absolute values of this parameter since this factor is introduced both for the calibration and for the measurements made in the neutron beam and will therefore cancel. However, if different electrometers are used a relative calibration factor will be required and any electrometer used should have its long-term stability checked periodically using a constant current supply.

$k_{t,p}$: *Temperature and pressure correction.* All chamber readings have to be converted to a reference temperature and pressure which are usually chosen to be those that are used by the standardizing laboratory at which the exposure chamber is calibrated.

$$k_{t,p} = \frac{T_m}{T_r}\frac{p_r}{p_m}$$

where T_r, T_m are respectively the reference and measurement absolute temperatures and p_r, p_m are the reference and measurement pressures. It should be noted that adequate time should be allowed for the chamber to reach the same temperature as its surroundings before a measurement is made. Also when gas flow is being used the temperature of the gas may be different from the temperature of the chamber. It is, therefore, advisable to ensure that the chamber, the phantom and the gas supply are all at room temperature before starting to take measurements.

k_s: *Correction for lack of saturation.* Saturation characteristics of the chamber should be determined by measuring charge as a function of applied voltage at the absorbed dose rate used for calibration.

In a continuous photon beam plotting $1/Q$ against $1/V^2$ should generally provide a linear fit to the data which can be extrapolated to infinite voltage. From this line the correction factor for the voltage which is routinely used can be interpolated. However, effects other than recombination may alter the voltage dependence of the collected charge. In particular there may be changes in collecting volume due to an inadequately designed guard ring which may make it necessary to use other powers of $1/V$ to produce a line which can be accurately extrapolated to infinite voltage. For neutrons, where the predominant effect is initial recombination, a plot of $1/Q$ against $1/V$ will be more appropriate.

k_l: *Correction for leakage current.* Leakage currents should not be a significant part of the ionization current and this should be investigated when the voltage is applied to the chamber and the radiation beam is off.

k_p: *Correction for polarity.* A change in polarity can cause a change in the measured charge, which should be small. If the polarity effect is caused by extra-cameral currents it is possible to take the mean of the charges measured at each polarity and use such a measurement to derive the polarity correction factor for measurements made at one polarity. However, if the same polarity effect is observed both in the neutron and photon beams any correction will tend to cancel.

k_f: *Correction for gas flow-rate.* Variations of ionization current with flow-rate should be assessed. These may be caused by diffusion of air into the chamber, which is most significant at low flow-rates, or by pressure build-up in the chamber at high flow-rates. It should be possible to operate the chamber in a gas flow-rate region where neither effect occurs although if this is not possible a correction factor should be determined. A check of adequacy of TE gas flow through the chamber can be made by comparing the reading with TE gas to that with dry air, which should be a ratio of 1.16 for the photons used for calibration.

k_h: *Correction for humidity.* If the standardizing laboratory provides a calibration factor for the exposure standard chamber for dry air, humidity corrections for unsealed air-filled chambers should be made. The curve representing $1/k_h$ as a function of relative humidity as presented in ICRU Report 31 (ICRU, 1979), is recommended to obtain the ionization appropriate to dry air. For a chamber flushed with the TE gas, k_h is equal to 1.

Πk_A is the product of several correction factors used to account for the finite size of the TE chamber, its build-up cap and stem, when measurements are made in air. These are not included in Πk_R because they are only valid for measurements in air, whereas Πk_R contains all the correction factors that are valid during measurements in air as well as in the phantom. Πk_A is a composite factor and equal to the product of the factors k_w, k_{st}, k_{rn} and k_{an}. Detailed information on these corrections factors can be found in Niatel *et al.* (1975).

k_w: *Wall and build-up cap correction factor.* This factor corrects for the attenuation and scattering caused by the wall and the build-up cap of the chamber. It may be investigated experimentally by measuring ionization current as a function of build-up thickness for thicknesses greater than that required for charged-particle equilibrium to be established. If these data are plotted and extrapolated to the mean centre of charged particle production, an estimate of this correction factor can be made. Monte Carlo calculations have recently been carried out by Nath and Schulz (1981) for a number of commercially available ionization chambers.

k_{st}: *Stem correction factor.* The effect of stem scatter on ionization current can be assessed by placing a dummy stem on the end of the chamber which is opposite to the true stem and measuring any change in the ionization current produced.

k_{rn}: *Radial non-uniformity correction factor.* A uniform calibration field should be used otherwise the photon fluence over the area of the chamber in the plane perpendicular to the axis of the beam will vary. Similar considerations have to be made when making measurements with the exposure standard chamber.

k_{an}: *Axial non-uniformity correction factor.*
Changes in photon fluence with distance from the source will be small because the chamber is usually calibrated at a fairly long SSD (> 50 cm). At these distances the error in assuming the effective centre to be at the geometrical centre can be ignored (Kondo and Randolph, 1960).

At the present time most national standards laboratories do not provide an absorbed dose calibration standard. If this were provided for calibration it could be used for direct calibration of the TE ionization chamber and would make it unnecessary to use the factors $(f_t)_c$ and $(\Pi k_A)_c$. It should be noted, however, that such a standard would be calibrated to give absorbed dose in water in a phantom at the position of the centre of the chamber when the chamber is replaced by the phantom material. This can be converted to the absorbed dose in reference tissue, $(D_t)_c$, by multiplying by $[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_{H_2O}]_c$. For the calibration of the TE chamber the absorbed dose in tissue adjacent to the cavity of the chamber is required. A displacement factor $(k_d)_c$ defined in an analogous way to $(k_d)_T$, as discussed in section 3.1, has to be applied. Measurements of $(k_d)_c$ are given in Johansson *et al.* (1978).

The calibration factor with photons a_c can now be written as:

$$a_c = \frac{(D_w)_c}{R_c(\Pi k_R)_c}\left[\frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_w}\right]_c \frac{1}{(k_d)_c}\,. \qquad (5.1\text{–}4)$$

The overall uncertainty in the determination of

TABLE 5–1
UNCERTAINTIES (IN %) IN THE DETERMINATION OF THE ABSORBED DOSE CALIBRATION FACTOR FROM AN EXPOSURE CALIBRATION IN AIR

Source	Symbol	Uncertainty
Reading of the chamber	R_c	0.2
Reading correction factors	$(\Pi k_R)_c$	0.3
Exposure	X_c	1.0
Exposure to absorbed dose factor	$(f_t)_c$	0.5
Correction factors for detector geometry	$(\Pi k_A)_c$	0.3
		Overall*: 1.2

*The overall uncertainty has been calculated by taking the square root of the sum of the squares of the separate uncertainties which are estimates of one standard error.

the absorbed dose calibration factor obtained from an exposure calibration in air is given in Table 5–1.

5.2. *Neutron absorbed dose measurement*

The physical parameters applied in determining D_N and D_G by means of equations (2–2) and (3.1–8) are a function of the neutron and photon spectrum and may vary with the position of the detector in the phantom. It is therefore recommended that all absorbed-dose determinations in the neutron beam are normalized to a measurement at the reference point where these parameters should be estimated. Analogous to photon beams in the energy range 1 to 10 MeV this point should be located at a depth of 5 cm from the front of the phantom surface along the central axis of the beam. A measurement should be made for each irradiation condition, *e.g.* field size and wedge filter (see Section 6.4).

The following procedure should be followed.

(a) *Phantoms.* For purposes of absorbed-dose standardization it is necessary to choose a well-defined and readily available material whose neutron attenuation properties are similar to those of muscle tissue over the broad range of neutron energies used in therapy.

It is recommended that water be used as the standard material for this purpose. It has the advantage over the fat-free muscle-equivalent liquid of Frigerio *et al.* (1972), which is used by the American groups, that water is also the medium on which a considerable body of information on the spatial distributions of absorbed dose in photon and electron therapy is based.

The phantom container should be made of a plastic material such as Perspex (Lucite) or polystyrene and the wall should be made thick enough (about 6 mm) to prevent flexing of the surface. A thinner window (about 3 mm) should be provided at the entrance surface so that ion chamber measurements at shallow depths are not significantly perturbed by the presence of the wall. The container should be deep enough to provide maximum backscatter and large enough in cross-sectional area to provide about a 5 cm margin around the largest field size for measurements of beam isodose contours. Generally, a $30\times30\times30$ cm^3 container will be large enough to eliminate phantom-size effects.

(b) *Position of measurement.* The geometrical centre of the detector shall be positioned at the reference point in the water phantom, placed at the nominal SSD.

(c) *Wall thickness.* The equilibrium wall thickness of an ion chamber for neutrons will generally not be the same as that for calibration photons. The depth of maximum dose varies from about 2 mm for d(16)+Be to about 8 mm of A-150 plastic for d(50)+Be neutron beams. Preferably a total wall thickness of A-150 plastic equal to this depth should be used. In practice it might be convenient to use the same A-150 build-up cap that would be used for the photon calibration. It is expected that for such a geometry the difference between A-150 plastic and water will not significantly influence the reading of the ion chamber.

(*d*) *Correction factors* k_R. The correction factors for temperature and pressure, leakage current, loss of ionization due to recombination, polarity effects, radiation sensitivity of the chamber stem and TE gas flow rate will generally be different for the neutron beams and for the γ rays used for calibration. Therefore these correction factors must be determined experimentally for the neutron beam as well, as discussed in Section 5.1. for the calibration photon beam.

(e) *Physical parameters.* The recommendations given in Section 4 shall be used to calculate D_N and D_G at the reference point.

The overall uncertainty in the determination of the total absorbed dose D_N+D_G in a neutron field, determined with a TE ion chamber using equation (3.1–9), is given in Table 5–2. The uncertainty in the physical parameters will in general be a function of the neutron energy. Estimated values are given in Table 5–2 for therapeutic neutron beams with average neutron energies higher than a few MeV. The uncertainty in the neutron kerma ratio increases with neutron energy. The overall uncertainty has been calculated by taking the square root of the sum of the squares of the separate uncertainties, which are estimates of one standard error.

6. Determination of Absorbed Dose at any Point

In principle relative absorbed dose distributions for neutron beams are determined in a similar way as for photon beams, the procedure for which can be found in relevant protocols. The main difference compared with the procedure applied for photon beams is that in neutron dosimetry the separate neutron and photon absorbed doses have to be determined. This implies that at any point the readings of two detectors have to be evaluated in order to obtain D_N and D_G at that point. These values should be related to the absorbed dose values at the reference point. It is generally assumed that the physical parameters applied to calculate D_N and D_G from the detector readings are independent of the position of the detector in the beam.

6.1. *Central-axis absorbed-dose distribution*

When measuring central-axis depth-dose curves by means of ionization chambers a displacement correction has to be made (see Section 4.4.). A multiplicative displacement correction factor cannot be used at depths close to the dose maximum. It is therefore recommended that a radial displacement is used. Suggested values are 0.3 r_i for d+T neutrons and 0.4 r_i for d(50)+Be neutrons, where r_i is the radius of the gas volume of the chamber.

The increase in absorbed dose at depths less than the build-up depth should be assessed by means of thin walled ionization chambers by adding layers of A-150 plastic.

A more extensive description of the determination of the central-axis absorbed-dose distributions has been given in ICRU Report 26. A survey of central-axis dose distributions of clinically employed neutron beams has recently been given by Mijnheer and Broerse (1979).

6.2. *Isodose distributions*

Central axis absorbed dose distributions are usually combined with transverse measurements at several depths to obtain isodose distributions. In principle the same methods for neutron beams as for photon beams may be employed, due to the great similarity in isodose curves. Separate isodose curves for neutrons as well as for photons have to be generated in the neutron beams. It will depend on the dose specification procedure if and at what stage these separate dose components should be combined.

ICRU Report 26 describes the influence of shielding and collimators on the separate neutron and γ-ray absorbed-dose beam profiles. Results of this type of measurement for clinically employed neutron beams have been recently summarized (Mijnheer and Broerse, 1979).

6.3. *Absorbed-dose specification*

Because of their significantly different biological effectiveness, the separate neutron and γ-ray dose components, D_N and D_G, should be determined as accurately as possible at all relevant positions, for different field sizes and irradiation conditions.

There are two aspects of dose specification, namely the prescription of absorbed dose given for daily radiotherapy treatments and the reporting of the absorbed doses at the conclusion of a patient's treatment. It is not practical to use two figures for the daily dose prescription so that a single parameter has to be used. Three alternatives are possible. Firstly, total absorbed dose, $D_N + D_G$, which is the system

TABLE 5–2

Uncertainties (in %) in the determination of the total absorbed dose in tissue in a neutron field with the aid of a TE ionization chamber

Source	Symbol	Uncertainty
Reading of the chamber	R_T	0.2
Reading correction factors	$(\Pi k_R)_T$	0.3
Displacement correction factor	$(k_d)_T$	0.5
Absorbed dose calibration factor	α_c	1.2
Ratio of average energy required to create an ion pair for A-150/TE gas chamber	W_N/W_c	4.0
Ratio of gas-to-wall absorbed dose conversion factor	$(r_{m,g})_N/(s_{m,g})_c$	2.0
Ratio of neutron kerma in tissue to that in the chamber wall	$(K_t/K_m)_N$	2.6 to 9.7*
Photon mass energy absorption coefficient ratio	$(\mu_{en}/\rho)/(\mu_{en}/\rho)_m$	0.1
		Overall†: 5.4 to 10.8*

*According to Bewley (1980). The lower value is valid for a d(16)+Be beam, the higher for a p(66)+Be beam.

†The overall uncertainty has been calculated by taking the square root of the sum of the squares of the separate uncertainties which are estimates of one standard error.

adopted by all American groups because this quantity can be assessed with the lowest overall uncertainty and the distribution can be measured with a single instrument. Secondly, neutron absorbed dose, D_N, can be used. Thirdly, total effective dose, $D_E = D_N + D_G/\tau$, has been introduced where τ is a weighting factor indicating the effectiveness of the neutron component compared with the γ-ray component for relevant effects on tumours and normal tissues. The European centres have followed all three procedures for dose prescription, with the value of τ being 3 for those groups using effective dose. Since the isodose distributions are similar for each of these systems, no recommendations are being made at the present time on the method to be used for combining the absorbed-dose components for daily prescriptions.

For the reporting of absorbed dose at the end of treatment it is necessary that both components are given. ICRU Report 29 (ICRU, 1978b) has made recommendations for the final reporting of external beam therapy with photons and electrons and where applicable these recommendations should be followed for external neutron beam therapy. In ICRU Report 29, the position has been defined at which the target absorbed dose should be specified. This definition should be followed for neutron dosimetry and at that position both components should be given. There are different ways in which these numbers can be quoted and it is recommended to give total absorbed dose with the γ absorbed dose in brackets. In some centres it is common clinical practice to specify the absorbed dose at a certain "total effective dose" isodose curve which surrounds the target area. According to the recommendations given in ICRU Report 29, this value should not be stated. It should be noted that the relative γ-ray contribution may vary over such a "total effective dose" isodose curve.

6.4. *Description of irradiation technique*

Specification of target absorbed dose alone is not sufficient for reporting. Information on the irradiation technique should be given to facilitate the comparison of biological and clinical results obtained with different neutron sources. The following information relevant to the irradiation conditions should be specified.

(a) *Radiation quality.* The principal factors affecting the neutron spectrum incident on a phantom should be specified. These are: the incident charged-particle type and energy, target material and target thickness, and the thickness and material of the filter in the primary neutron beam. The notation p(66)+Be(49)−6 cm polyethylene can be used where 66 MeV protons are incident on a Be target in which they loose only 49 MeV and where the resultant neutron beam is filtered by 6 cm of polyethylene. In the case of a thick target and no filtration this can be abbreviated to p(66)+Be.

(b) *Geometrical conditions.* Information on the geometrical conditions of irradiation should be provided, *e.g.* the number and arrangements of the beams, source to surface distance, patient positioning, etc.

(c) *Field size.* The field size, which is determined by the combination of various pertinent parameters, including neutron energy, collimator size, field shaping devices, distance, etc., can be significantly expressed only in terms of the dose distributions achieved in a tissue-equivalent phantom. The geometrical field size usually corresponds to the dimensions of the plane figure described by the intersection of the 50% isodose surface and the plane that passes through, and is normal to, the central axis at the location of the relative dose maximum. In institutes where it is common practice to apply a different beam definition for photon or electron treatment, it will be more suitable to use this definition also for the neutron treatment although this must be clearly stated. Agreement between the size and position of the neutron beam and optical mechanical beam-localizing devices should be established, *e.g.* by means of radiographic film (Dutreix *et al.*, 1978). Where relevant, the absorbed dose to shielded sites should be specified.

(d) *Beam modifying devices.* Information on wedges, filters and shielding blocks should be given. The effect of such modification on field uniformity should be determined.

(e) *Corrections for tissue heterogeneity.* It should be stated whether or not such corrections have been applied. It is recommended that these corrections be based on actual measurements in simulated configurations.

(f) *Time-dose patterns.* At least the number of fractions, *N*, and the overall treatment time, *T* (in days), should be given. If NSD calculations are made for neutron treatments, it should be stated what exponents for *N* and *T* are used. It should also be clear if the formula has been applied to the neutron absorbed dose, the total absorbed dose or the "total effective dose". Information on the target absorbed dose rate is useful.

7. CHECK OF ABSORBED DOSE GIVEN TO A PATIENT

The absorbed dose given to each patient shall be under proper control. The methods described for beams of X or γ rays (ICRU, 1976) are in general also valid for neutron beams. For this purpose dual absorbed-dose monitoring systems and measurements of the absorbed dose on patients are recommended (NACP, 1980).

7.1. *Absorbed-dose monitoring system*

The neutron beam should be continuously monitored by two independent systems, both deriving their signals from the beam itself. An additional check could be the accelerated charged-particle beam current on target. The integrated current in a transmission monitor chamber should determine the accumulated absorbed dose if technically possible. The design of the integrator circuit is important for accuracy of control. A well-designed circuit will make possible the display of both dose rate and also the integrated total dose delivered. Saturation of the collection current should be specifically checked. If the chamber is not sealed, a convenient procedure for correction for temperature, pressure and humidity should be established. It is essential that linearity and dose-rate independence be established as well as the relationship between monitor response and absorbed dose and beam output with field size. A calibration check of all monitoring detectors should be made regularly. If more than one monitor system is used the ratio of the monitors will give an indication of unsatisfactory performance.

The absorbed dose at the reference point in the primary phantom should be related to the monitor reading. For check measurements, however, it may be more convenient to use a simple test geometry, with the purpose of measuring the constancy of the monitor. For d+T neutron generators and low-energy cyclotrons a measurement in air will be easy, whereas for higher neutron energies a measurement with an ionization chamber at a fixed depth in a solid phantom of convenient size and material under specified conditions can be useful. Tissue-equivalent plastic and acrylic plastic phantoms can be used to supplement the primary phantom for source output consistency checks, and for intercomparison of ion chamber or other dosimetry systems. It is specifically recommended that TE plastic be used as the dose build-up material in those situations where the use of water is not feasible.

7.2. In-vivo *dosimetry*

An ultimate check of the actual treatment given can only be made by using *in-vivo* dosimetry. Entrance dose, exit dose and intracavitary or organ dose measurements are described in ICRU Report 24 (1976), for irradiation of patients with beams of X or γ rays. The detectors described, small condenser ionization chambers, TLD and small semiconductor detectors are in principle also useful in neutron beams if suitable detector materials are chosen. In addition the use of activation of small metal pellets has been reported for *in-vivo* dosimetry during fast neutron radiotherapy. The criteria when *in-vivo* dosimetry should be applied are the same for neutron therapy as for irradiations with photon beams. Because there is less experience with neutron therapy machines than with photon beams, it is useful, especially during the first period of clinical use of a new neutron therapy unit, to use patient dosimetry systems routinely. In these situations it is recommended that *in-vivo* dosimetry measurements are made at one of the first treatment occasions and always when the characteristics of the beam have been changed.

8. Dosimetry Intercomparisons between Institutions

Institutions engaged in neutron beam therapy should periodically carry out neutron dosimetry intercomparisons. The purpose of these intercomparisons is to verify the institutions' conformity to quantitative dosimetry standards and to serve as a review of the procedures and techniques employed for neutron dosimetry.

The intercomparison measurements should include neutron and photon absorbed dose determination. The use of a calibrated tissue-equivalent ionization chamber in combination with a dosimeter which is relatively insensitive to neutrons (k_U preferably lower than 0.15) is recommended for this purpose. Specific parameters that should be intercompared are:

(a) calibration of the dosemeters in a γ-ray field whose calibration is traceable to a national standards laboratory;

(b) determination of the dosemeter readings in the neutron beam relative to their sensitivities to the γ rays used for the photon calibration; these measurements shall be in air and at a few depths in the primary water phantom.

All measurements should be normalized to a carefully maintained and checked monitoring system.

The relative readings of the dosemeters in the neutron beam will be used to calculate the tissue kerma in free air and absorbed dose in the phantom for neutrons and photons using a common set of physical parameters.

Standardized measurement and correction procedures, as outlined in the preceding sections of this protocol, should be used. It is important to ascertain if significant systematic differences exist in the results.

Documentation of the intercomparison measurements should include a brief description of the γ-ray field and the neutron source, measurement techniques, the dosemeter readings and the physical parameters appropriate to the radiation field which are used to convert dosemeter readings to absorbed dose calibration factor, to kerma free-in-air or to absorbed dose in a phantom.

REFERENCES

AAPM, 1980. Protocol for neutron beam dosimetry. *AAPM Report No. 7*, (American Institute of Physics, New York).

Almond, P. R. and Smathers, J. B., 1977. Physics intercomparisons for neutron radiation therapy. *International Journal of Radiation Oncology Biology and Physics*, *3*, 169.

Amols, H. I., Dicello, J. F., Awschalom, M., Coulson, L., Johnsen, S. W. and Theus, R. B., 1977. Physical characterization of neutron beams produced by protons and deuterons of various energies bombarding beryllium and lithium targets of several thicknesses. *Medical Physics*, *4*, 486.

August, L. S., Theus, R. B. and Shapiro, P., 1978. Gamma measurements with a non-hydrogenous Rossi Counter in a mixed field. In *Proceedings of the Sixth Symposium on Microdosimetry, EUR 6064*, Ed. by J. Booz and H. G. Ebert. (Harwood Academic Publishers), p. 441.

Bewley, D. K., 1980. Practical kerma values for therapy applications. In *Monograph on Ion Chambers for Neutron Dosimetry, EUR 6782*, Ed. by J. J. Broerse. (Commission of the European Communities, Luxembourg), p. 209.

Bichsel, H. and Rubach, A., 1978. Uncertainty of the determination of absolute neutron dose with ionization chambers. In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine, EUR 5848*, Ed. by G. Burger and H. G. Ebert. (Commission of the European Communities, Luxembourg), p. 549.

Booz, J., 1979. Neutron dosimetry, radiation quality and biological dosimetry. In *High LET Radiations in Clinical Radiotherapy* (*Supplement to European Journal of Cancer*) Pergamon Press, Oxford), p. 147.

Broerse, J. J., 1980. (*Ed.*) *Monograph on Ion Chambers for Neutron Dosimetry, EUR 6782.* (Commission of the European Communities, Luxembourg).

Broerse, J. J., Burger, G. and Coppola, M., 1978. *A European Neutron Dosimetry Intercomparison Project (ENDIP). Results and Evaluation. EUR 6004.* (Commission of the European Communities, Luxembourg).

Broerse, J. J. and Mijnheer, B. J. 1976. Second draft protocol for neutron dosimetry. In *Basic Physical Data for Neutron Dosimetry. EUR 5629*, Ed. by J. J. Broerse. (Commission of the European Communities, Luxembourg), p. 311.

Broerse, J. J. and Mijnheer, B. J., 1981. Progress in neutron dosimetry for biomedical applications. In *Progress in Medical Radiation Physics* (Plenum Press, New York), (in press).

Broerse, J. J., Mijnheer, B. J., Eenmaa, J. and Wootton, P., 1979. Dosimetry intercomparisons and protocols for therapeutic applications of fast neutron beams. In *High-LET Radiations in Clinical Radiotherapy*, (*Supplement to European Journal of Cancer*). (Pergamon Press, Oxford), p. 117.

Caswell, R. S., 1960. Neutron-insensitive proportional counter for gamma-ray dosimetry. *Review of Scientific Instruments*, *31*, 869.

1966. Deposition of energy by neutrons in spherical cavities. *Radiation Research*, *27*, 92.

Caswell, R. S. and Coyne, J. J., 1972. Interaction of neutrons and secondary charged particles with tissue: secondary particle spectra. *Radiation Research*, *52*, 448.

Caswell, R. S., Coyne, J. J. and Randolph, M. L., 1980. Kerma factors for neutron energies below 30 MeV. *Radiation Research*, *83*, 217.

Dutreix, A., Bridier, A. and Wambersie, A., 1978. Is film dosimetry reliable for clinical applications of high energy neutron beams? In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine, EUR 5848*, Ed. by G. Burger and H. G. Ebert. (Commission of the European Communities, Luxembourg), p. 645.

Eenmaa, J. and Wootton, P., 1978. Protocol for neutron beam dosimetry. (Unpublished).

Frigerio, N. A., Coley, R. F. and Sampson, M. J., 1972. Depth dose determinations. I. Tissue-equivalent liquids for standard man and muscle. *Physics in Medicine and Biology*, *17*, 792.

Goodman, L. J., 1978. Density and composition uniformity of A–150 tissue equivalent plastic. *Physics in Medicine and Biology*, *23*, 753.

Goodman, L. J. and Coyne, J. J., 1980. W_n and neutron kerma for methane-based tissue-equivalent gas. *Radiation Research*, *82*, 13.

Heintz, P. H., Johnsen, S. W. and Peek, N. F., 1977. Neutron energy spectra and dose distribution spectra of cyclotron-produced neutron beams. *Medical Physics*, *4*, 250.

Hough, J. H., 1979. A modified lead attenuation method to determine the fast neutron sensitivity k_U of a photon dosimeter. *Physics in Medicine and Biology*, *24*, 734.

Hubbell, J. H., 1977. Photon mass attenuation and mass energy-absorption coefficients for H, C, N, O, Ar, and seven mixtures from 0.1 keV to 20 MeV. *Radiation Research*, *70*, 58.

ICRU, 1964. *Physical Aspects of Irradiation. International Commission on Radiation Units and Measurements.* Report 10b, 1962 (National Bureau of Standards Handbook, Washington, DC).

1976. *Determination of Absorbed Dose in a Patient Irradiated by Beams of X or Gamma Rays in Radiotherapy Procedures*, Report 24 (International Commission on Radiation Units and Measurements, Washington, DC).

1977. *Neutron Dosimetry for Biology and Medicine*, Report 26 (International Commission on Radiation Units and Measurements, Washington, DC).

1978a. *An International Neutron Dosimetry Intercomparison*, Report 27 (International Commission on Radiation Units and Measurements, Washington, DC).

1978b. *Dose Specification for Reporting External Beam Therapy with Photons and Electrons*, Report 29 (International Commission on Radiation Units and Measurements, Washington, DC).

1979. *Average Energy Required To Produce An Ion Pair*, Report 31 (International Commission on Radiation Units and Measurements, Washington, DC).

Ito, A., 1978. Neutron sensitivity of C-CO$_2$ and Mg-Ar ionization chamber. In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine. EUR 5848*, Ed. by G. Burger and H. G. Ebert. (Commission of the European Communities, Luxembourg), p. 605.

Johansson, K-A., Mattsson, L. O., Lindborg, L. and Svensson, H., 1978. Absorbed dose determination with ionization chambers in electron and photon beams with energies between 10 and 50 MeV. In *Proceedings of the International Symposium on National and International Standardization of Radiation Dosimetry*, IAEA-SM-222/35. (International Atomic Energy Agency, Vienna), p. 243.

Kondo, S. and Randolph, M. L., 1960. Effect of finite size of ionization chambers on measurements of small photon sources. *Radiation Research*, *33*, 37.

McDonald, J. C., Laughlin, J. S. and Freeman, R. E., 1976. Portable tissue-equivalent calorimeter. *Medical Physics*, *3*, 80.

Maier, E. and Burger, G., 1978. Experimental correction factors for chamber dosimetry. In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine. EUR 5848*, Ed. by G. Burger and H. G. Ebert.

(Commission of the European Communities, Luxembourg), p. 165.

Makarewicz, M. and Pszona, S., 1978. Theoretical characteristics of a graphite ionization chamber filled with carbon dioxide. *Nuclear Instruments and Methods, 153,* 423.

Meulders, J. P., Leleux, P., Macq, P. C. and Pirart, C., 1975. Fast neutron yields and spectra from targets of varying atomic number bombarded with deuterons from 16 to 50 MeV. *Physics in Medicine and Biology, 20,* 235.

Mijnheer, B. J., 1980. The relative neutron sensitivity, k_U, for nonhydrogenous detectors. In *Monograph on Ion Chambers for Neutron Dosimetry, EUR 6782,* Ed. by J. J. Broerse. (Commission of the European Communities, Luxembourg) p.307.

Mijnheer, B. J. and Broerse, J. J., 1979. Dose distributions of clinical fast neutron beams. In *High-LET Radiations in Clinical Radiotherapy,* (*Supplement to European Journal of Cancer*). (Pergamon Press, Oxford), p. 109.

Mijnheer, B. J., Visser, P. A., Lewis, V. E., Guldbakke, S. Lesiecki, H., Zoetelief, J. and Broerse, J. J., 1979. The relative neutron sensitivity of Geiger-Müller counters. In *High-LET Radiations in Clinical Radiotherapy,* (*Supplement to European Journal of Cancer*). (Pergamon Press, Oxford), p. 162.

Mijnheer, B. J. and Williams, J. R., 1981. Determination of absorbed dose and kerma in a neutron field from measurements with a tissue-equivalent ionization chamber. *Physics in Medicine and Biology, 26,* 57.

NACP, 1980. Procedures in External Radiation Therapy Dosimetry with Electron and Photon Beams with Maximum Energies Between 1 and 50 MeV. *Acta Radiologica, Oncology Radiation Physics and Biology, 19,* 55.

Nath, R. and Schulz, R. J., 1981. Calculated response and wall correction factors for ionization chambers exposed to ^{60}Co gamma-rays. *Medical Physics, 8,* 85.

Niatel, M-T., Loftus, T. P. and Oetzmann, W., 1975. Comparison of exposure standards for ^{60}Co gamma-rays. *Metrologia, 11,* 17.

Parnell, C. J., 1972. A fast neutron spectrometer and its use in determining the energy spectra of some cyclotron-produced fast neutron beams. *British Journal of Radiology, 45,* 452.

Pearson, D. W., Attix, F. H., DeLuca, P. M. Jr., Goetsch, S. J. and Torti, P. P., 1980. Ionization error due to porosity in graphite ionization chambers. *Physics in Medicine and Biology, 25,* 333.

Porter, D., Lawson, R. C. and Hannan, W. J., 1975. A novel fast neutron dosemeter based on fission chambers. I: Principles of operation and theoretical response in neutron therapy radiation fields. *Physics in Medicine and Biology, 20,* 431.

Rossi, H. H. and Failla, G., 1956. Tissue-equivalent ionization chambers. *Nucleonics, 14,* 32.

Shapiro, P., Attix, F. H., August, L. S., Theus, R. B. and Rogers, C. C., 1976. Displacement correction factor for fast-neutron dosimetry in a tissue-equivalent phantom. *Medical Physics, 3,* 87.

Smathers, J. B., Otte, V. A., Smith, A. R., Almond, P. R., Attix, F. H., Spokas, J. J., Quam, W. H. and Goodman, L. J., 1977. Composition of A-150 tissue-equivalent plastic. *Medical Physics, 4,* 74.

Smith, A. R., Almond, P. R., Smathers, J. B., Otte, V. A., Attix, F. H., Theus, R. B., Wootton, P., Bichsel, H., Eenmaa, J., Williams, D., Bewley, D. K. and Parnell, C. J., 1975. Dosimetry intercomparisons between fast-neutron radiotherapy facilities. *Medical Physics, 2,* 195.

Wagner, E. B. and Hurst, G. S., 1961. A Geiger-Müller gamma-ray dosimeter with low neutron sensitivity. *Health Physics, 5,* 20.

Waterman, F. M., Kuchnir, F. T., Skaggs, L. S., Kouzes, R. T. and Moore, W. H., 1979. Energy dependence of the neutron sensitivity of C-CO$_2$, Mg-Ar, and TE-TE ionization chambers. *Physics in Medicine and Biology, 24,* 721.

Weaver, K., Bichsel, H., Eenmaa, J. and Wootton, P., 1977. Measurement of photon dose fraction in a neutron radiotherapy beam. *Medical Physics, 4,* 379.

Zoetelief, J., Engels, A. C., Broerse, J. J. and Mijnheer, B. J., 1980. Effect of finite size of ion chambers used for neutron dosimetry. *Physics in Medicine and Biology, 25,* 1121.

Appendix I

List of Symbols

a_c	calibration factor with photons for a tissue-equivalent ionization chamber
δ	fractional error introduced when a tissue-equivalent ionization chamber alone is used to measure the total absorbed dose
$\mathrm{D_m}^*$	absorbed dose in the wall material adjacent to the cavity of the chamber
D_t	absorbed dose in tissue
e	charge of the electron
f_t	factor required to convert exposure to absorbed dose in tissue
h_T, h_U	sensitivity of a dosemeter to photons in a mixed field relative to its sensitivity to the γ rays used for calibration.
K	kerma
Πk_A	the product of several correction factors to account for the finite size of the chamber, its build-up cap and stem when making measurements in air, including:
	k_w wall and build-up cap correction factor
	k_{st} stem correction factor
	k_{rn} radial non-uniformity correction factor
	k_{an} axial non-uniformity correction factor
k_d	Displacement correction factor
Πk_R	The product of several correction factors to correct the reading of an ionization chamber, R, to the charge produced in the cavity, Q, including:
	k_e electrometer calibration factor
	$k_{t,p}$ temperature and pressure correction
	k_s correction for lack of saturation
	k_l correction for leakage current
	k_p correction for polarity
	k_f correction for gas flow rate
	k_h correction for humidity
k_T, k_U	sensitivity of a dosemeter to neutrons relative to its sensitivity to the γ rays used for calibration
m	mass of the gas in the cavity
μ_{en}/ρ	mass energy absorbtion coefficient
N_e	exposure calibration factor
Q	total charge produced within the cavity of an ionization chamber
R	reading of a dosemeter
R′	quotient of the reading of a dosemeter by its sensitivity to the γ rays used for calibration
r_i	radius of the gas cavity of an ionization chamber
$r_{m,g}$	gas-to-wall absorbed dose conversion factor for ionization chambers
$s_{m,g}$	mass stopping powers of the wall relative to the gas of the particles produced in the wall of an ionization chamber
τ	weighing factor indicating the relative effectiveness of the neutron component
W	average energy required to produce an ion pair
X	exposure

Appendix II

Code of Practice for Clinical Neutron Dosimetry

C.1 *Instrumentation*

A tissue-equivalent ionization chamber constructed of A-150 plastic and filled with TE gas (64.4% CH$_4$, 32.4% CO$_2$ and 3.2% N$_2$ by partial pressure) should be used. A common instrument for the ECNEU groups is the Exradin T-2 chamber. This instrument can be considered to measure the total absorbed dose in the neutron beam.

For the photon component of the neutron beam a Geiger-Müller counter is recommended due to its low k_U value. It should have an energy compensating shield as described by Wagner and Hurst (1961) and should be surrounded with a thermal-neutron absorbing shield. ^{6}Li is suggested either in the form of ^{6}Li metal or ^{2}LiF powder with a thickness of at least 0.3 g cm^{-2}. The dead time of the tube should be determined so that the measurements can be corrected for this.

If it is impractical to use a GM counter, a non-hydrogenous ionization chamber can be used. This should preferably be a Mg-Ar chamber.

C.2 *Photon calibration*

Calibration of the TE dosemeter should be made in air either in a ^{60}Co, 2 MV or ^{137}Cs beam. An exposure standard chamber should be used which has a calibration factor traceable to a national standards laboratory. The calibration factor with photons of the TE chamber is given by:

$$a_c = \frac{X_c(f_t)_c(\Pi k_A)_c}{R_c(\Pi k_R)_c}$$

$$\text{where } (f_t)_c = \frac{(W_{air})_c}{e}\left[\frac{(\mu_{en}/\rho)_t}{(\mu_{en}/\rho)_{air}}\right]_c$$

$(\Pi k_R)_c$ is the product of the experimental correction factors to be applied to the TE chamber which are specific to that chamber and the measurement conditions. These factors include correction for temperature and pressure, lack of saturation, leakage current, polarity effects and gas flow. Numerical values for some chambers at some neutron energies were discussed during the workshop on Ion Chambers for Neutron Dosimetry (Broerse, 1980).

$(\Pi k_A)_c$ is the product of the correction factors which account for the finite size of the chamber during the measurements in air. These include corrections for the attenuation and scatter within the wall and build-up cap of the chamber, correction for stem scatter and for field non-uniformity. The wall and build-up correction factors should be taken from Nath and Schulz (1981).

X_c/R_c is the ratio of exposure measured by the standard chamber to the reading of the TE ionization chamber.

The units of a_c are Gy C^{-1}; if the units of X are R an additional numerical factor 2.58×10^{-4} is required.

Values of the parameters to be used for the different calibration energies are given in Table C-1.

TABLE C-1

PARAMETERS REQUIRED FOR CALIBRATION OF TE IONIZATION CHAMBER

Parameter	Energy	Value
$(W_{air})_c/e$		33.85 JC^{-1}
$[(\mu_{en}/\rho)_t/(\mu_{en}/\rho)_{air}]_c$*	^{60}Co	1.103
	2 MV	1.102
	^{137}Cs	1.103
$(f_t)_c$	^{60}Co	9.63×10^{-3} Gy R^{-1}
	2 MV	9.62×10^{-3} Gy R^{-1}
	^{137}Cs	9.63×10^{-3} Gy R^{-1}

*Data taken from Hubbell (1977).

The GM counter should be calibrated in a similar manner in air in either a ^{60}Co or a ^{137}Cs beam, which should be indicated. The dose rate should be sufficiently low (smaller than about 2 mGymin^{-1}) so as to give a small dead time correction.

C.3 *Neutron beam measurements and dose specification*

Neutron and photon absorbed-dose distributions should be calculated from measurements made with the TE chamber and GM counter in a phantom. A water-filled phantom with minimum dimensions of $30 \times 30 \times 30$ cm^3 should be used. Absolute measurements of neutron and photon absorbed dose should be made for one field size at a reference depth of 5 cm, all other doses being related to that reference measurement. Doses close to the surface may have to be found by extrapolation.

Calculation of the separate absorbed dose components is made by solving the simultaneous equations:

$$R_T(\Pi k_R)_T(k_d)_T\, a_c = k_T D_N + h_T D_G$$

$$R_U' = k_U D_N + h_U D_G$$

Many of the constants required for neutron dosimetry are dependent on the neutron energy spectrum and can only be calculated if that spectrum is known. In many instances spectra need not be measured for a specific source since published data may be adequate. For d+T neutrons it is sometimes sufficient to assume that even in a phantom the

TABLE C-2

PARAMETERS REQUIRED FOR DETERMINATION OF ABSORBED DOSE IN TISSUE IN THE NEUTRON BEAM AT THE REFERENCE POINT

Parameter		Value	Reference
k_T:	W_c/e	29.3 JC^{-1}	Goodman and Coyne, 1980
	W_N/e	(31.1–31.3)* JC^{-1}	Goodman and Coyne, 1980
	$(s_{m,g})_c$	1.00	
	$(r_{m,g})_N$	0.99	
	$[(\mu_{en}/\rho)_t/(/_{en}/\rho)_m]_c$	1.001	For ^{60}Co, 2 MV or ^{137}Cs Hubbell (1977)
	$(K_t/K_m)_N$	(0.95–0.98)*	Caswell *et al.* (1980)
k_U:	GM counter	(0.005–0.025)*	Mijnheer *et al.* (1980)
	Mg/Ar chamber	(0.07–0.17)	Mijnheer (1980)
h_T:		1.00	
h_U:		1.00	
$(k_d)_T$:		$1-2.5 \times 10^{-3} r_1$† (r_1 in mm)	Zoetelief *et al.* (1980)

*Value of parameter is dependent on neutron spectrum. Values given indicate approximate range of values for the neutron sources used by the ECNEU groups.

†For relative measurements in a phantom the geometrical centre of the chamber should be shifted by ¼ radius of the cavity away from the source to account for the displacement of the effective centre of measurement.

beam is monoenergetic although in-phantom spectrum data would give more accurate values. For neutron beams produced by deuterons with an energy of approximately 15 MeV on a thick beryllium target the spectrum of Parnell (1972) may be used provided that the neutron energies are scaled by the ratio of the user's deuteron energy to that used by Parnell (16.7 MeV). At higher energies, and for different incident particles and targets, spectrum data have been published by many authors, in particular Meulders *et al.* (1975), Heintz *et al.* (1977), Amols *et al.* (1977). However, measurement of the user's own spectrum both in air and at different positions in a phantom should be encouraged.

Values of the parameters to be used, or references for the values of the energy dependent parameters, are given in Table C-2.

For neutron therapy treatments, dose may be prescribed as neutron absorbed dose (D_N), total absorbed dose ($D_N + D_G$) or total effective dose (D_E). In the summary of the treatment and when reporting the clinical results of neutron therapy, the target absorbed dose as specified in ICRU Report 29 should be included with the two components given separately. It is recommended that this statement should be in the form of total absorbed dose with the γ-ray absorbed dose in brackets. Also the other recommendations given in that report should be followed in reporting absorbed doses in external neutron-beam therapy.

Book reviews

The Effects on Populations of Exposure to Low Levels of Ionizing Radiation. Revised edit. Report of the committee on the Biological Effects of Ionizing Radiations: National Research Council, pp. 524, 1980 (National Academy Press, Washington DC), $14.25.
ISBN 0-309-03095-1

A weighty and important document representing the final form of the BEIR III report, the earlier version of which (1979) raised much controversy.

Based on a very extensive literature survey, a large and broadly-based committee has attempted to update the previous reports and to provide reasonable estimate of risk for genetic and somatic effects in populations exposed to low levels of ionizing radiation.

The report begins with a general summary and an introduction which presents the historical background and outlines the committee's brief.

The first main section (II, pp. 11–36) supplies basic physics and radiobiology, and pays particular attention to the mathematical theory of dose-response curves and their application for making risk estimates. Section III (pp. 37–70) lists and estimates the sources and rates of low-level radiation exposure to which the population of USA is likely to be exposed.

The next section (IV, pp. 71–134) deals with the genetic effects of radiation and the health consequences arising from them. Two methods are used to estimate risk, one providing an "equilibrium" value for continuous exposure over many generations, the other a more direct estimate of the incidence expected within a single generation following parental exposure. Both estimates are in good agreement.

The largest section, constituting more than half of the report, is devoted to somatic effects: cancer (V, pp. 135–476), which the committee considers to be the most important somatic effect of exposure to low-level ionizing radiation. This is perhaps the most controversial section, and sharp divisions of opinion within the committee have led to the inclusion of a number of dissenting appendices by individual members including the chairman! Since cancer is a relatively common naturally-occurring phenomenon, and radiation-induced cancer cannot be distinguished by particular characteristics, excess incidence above the natural level relies heavily on statistical inference. Add to this the fact that natural incidence varies with many factors like age, sex, ethnic origin, locality etc; that radiosensitivity varies from organ to organ; that almost nothing is known about the mode of induction or the form of the dose response curve, then it is not surprising that controversy exists. The report weaves its way through all the various ramifications of the problem, drawing on extensive data (cited in an appendix and usefully classified according to site of incidence) and deriving various risk estimates for incidence and mortality. The committee has obviously been at pains to allay criticisms levelled at previous reports, and has sought to explore and comment on every avenue. The result makes very hard reading, but the scope of the data and discussions produce a veritable mine of useful information and ideas.

Section VI considers somatic effects other than cancer, and is concerned principally with pre-natal exposure and developmental effects produced *in utero*.

The report is more a work of reference than a text book, although useful summaries are placed at strategic places, and the more complex and erudite arguments are presented in notes at the ends of the sections. The paucity of human data on which to base good estimates is frequently highlighted, but the committee has made a serious and careful attempt to extrapolate from available animal data. Unfortunately, only time will tell if the estimates so obtained are a valid basis for radiation protection standards for the population.

J. R. K. SAVAGE.

Cancer. By Thomas J. Deeley, pp. 32, 1980 (Alpha and Omega Publishing Co., Cardiff), 40p.

This small booklet of thirty-two pages explains in very simple terms some of the important facts about cancer. It is particularly suitable for persons such as medical records staff, receptionists, medical social workers and others such as voluntary hospital workers who might wish to increase their understanding about patients.

It is well illustrated by simple diagrams and is easily understood. It is published for the Tenovus Cancer Information Centre and any proceeds from sales will be used to support work in Cardiff.

BRENDAN HALE.

1981, *British Journal of Radiology*, 54, 899–904 OCTOBER 1981

Dose-effect relations for tumour control and complication rate after fast neutron therapy for pelvic tumours

By J. J. Battermann, G. A. M. Hart and K. Breur

Radiotherapy Department, Antoni van Leeuwenhoek Hospital (The Netherlands Cancer Institute), Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

(Received November 1980)

ABSTRACT

The effects of fast neutrons and high-energy photons were analysed for tumour control and skin and bowel damage after treatment of bladder and rectal cancers. A combination of statistical models was used for this analysis. A steep dose-effect curve was found for local tumour control as well as for the risk of complications. Some estimates were made of RBE values for control of bladder tumour and for normal-tissue damage. The implication of these data for neutron therapy is discussed.

Fast neutron therapy has been used in Amsterdam since November 1975 as a routine treatment modality for advanced tumours in different regions of the body. Preliminary results of some pilot studies have been presented elsewhere (Battermann and Breur, 1979). For irradiations in the pelvis two parallel-opposed beams were used. Because of the relatively poor depth-dose characteristics of our d+T neutron generator (Mijnheer *et al.*, 1978) the maximum dose was about 20% higher than the dose at the mid-line. This high dose administered to the skin and intestine allowed us to score the effects of fast neutrons on these normal tissues over a wide range of dosages. Comparison of these results with available data on megavoltage photon irradiation for bladder tumours made it possible to estimate RBE values for skin and intestinal damage and for control of bladder tumour.

In this paper the dose-effect relations for tumour control and complication rate after fast neutron therapy for pelvic tumours are discussed.

METHODS AND MATERIALS

In the Antoni van Leeuwenhoek Hospital fast-neutron teletherapy is given with the 14 MeV Philips neutron generator. The sealed-off d+T neutron tube is placed in a Brown-Boveri betatron gantry, providing isocentric radiation facilities. At a SSD of 80 cm the dose rate in a water phantom at 10 cm depth is about 4 cGy/min for a 10×10 cm^2 field size. The γ component of the beam at that depth is about 10% of the total absorbed neutron and γ dose rate. Twelve collimators are available, providing field sizes from 6×6 cm^2 to 16×23 cm^2 at 80 cm SSD. For pelvic irradiation a field size of 13×16 cm^2 is usually applied. The collimator opening is covered with a 0.5 mm sheet of lead, thus avoiding any proton contamination of the beam (Mijnheer *et al.*, 1978).

In the literature a diversity of descriptions of neutron dose can be found. So, at the Hammersmith Hospital neutrons only (D_N) are quoted (Catterall and Bewley, 1979). In the US centres the dose is expressed as total dose: neutron dose plus contaminating γ dose ($D_N+D_G=D_T$). Often this total dose is converted into a "photon equivalent" dose by multiplying the neutron dose with the appropriate RBE (Peters *et al.*, 1979). The use of a "total effective dose" (TED) (Duncan and Arnott, 1979), defined as neutron dose plus one third of the γ dose ($D_N+D_G/3$), seems a simple and practical way of stating the biologically effective dose. However, the value of 1/3 as the approximate normal-tissue RBE of the contaminating γ rays was determined at much higher dose levels than the few cGy per fraction contaminating the neutron beam (Denekamp, 1980). To make intercomparisons of treatments at different centres feasible, the quotation of total dose with the γ dose in brackets is recommended. Of course, the variation of RBE with neutron energy also has to be taken into account when results at different centres are compared. In this study, all dosages are quoted as total dose.

Data from 66 patients treated from November 1976 to December 1979 were used for this analysis. Initially, fast neutron irradiation was given with two parallel-opposed fields. Due to the relatively poor depth-dose distribution (Fig. 1) of the beam, in some areas the dose was found to be 20% higher than at the mid-line. In addition, the dose given was almost 8% higher than intended. The difference was caused by reconsideration of some physical parameters in dosimetric measurements (Zoetelief *et al.*, 1979). Since 1978 a six-field technique has been used and thus a more homogeneous dose distribution can be achieved (Fig. 2).

As the high-dose areas happened to be subcutaneous tissues and parts of the small bowel and rectosigmoid colon, the effects of neutron irradiation on these normal tissues could be scored over a wide

TABLE I

SCORING SCALE FOR REACTIONS OF TUMOURS AND NORMAL TISSUES IN THE PELVIS

Score	Tumour regression	Skin and subcutaneous tissues	Intestinal tissues
0	Complete regression	No reactions	No reactions
1	Partial regression, > 50% of tumour volume	Depigmentation, atrophy	Some bowel inconvenience
2	Partial regression, < 50% of tumour volume	Mild fibrosis	Reactions requiring conservative medical care
3	No regression	Severe fibrosis, shrinking > 1/3 of treated area	Severe reactions requiring surgical care (colostomy)
4	Tumour progression	Necrosis, death due to complications	Necrosis, bowel perforation, death due to complications

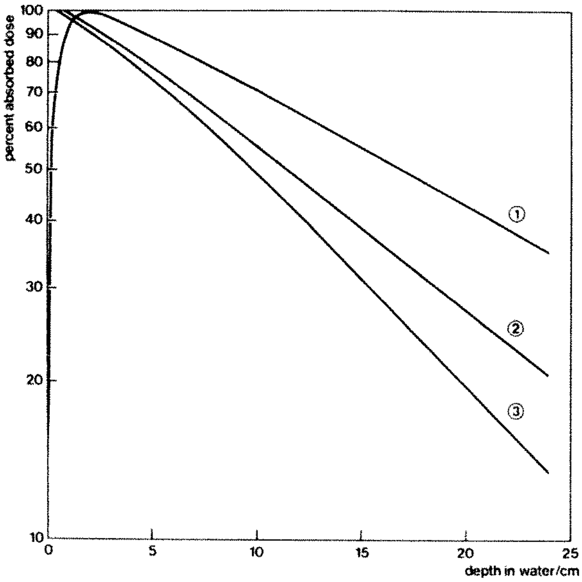


FIG. 1.

Central axis depth dose curves for 8 MV X rays (1), ^{60}Co γ rays (2) and 14 MeV neutrons (3) for field sizes of approximately 10×10 cm^2.

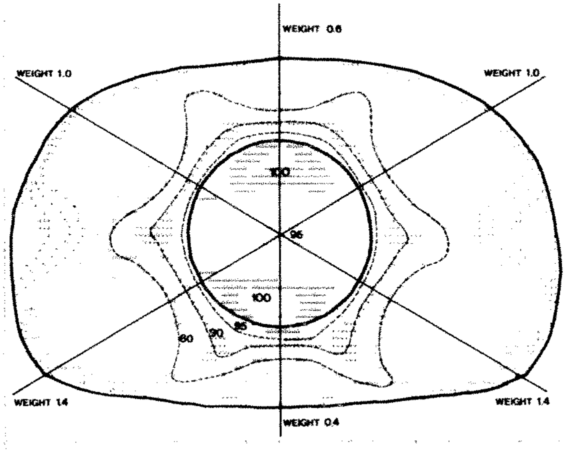


FIG. 2.

Computed isodose curves for a six-field irradiation of pelvic tumours.

range of dosages. Although a five point scale (Table I) was used to score the radiation effects, for a meaningful statistical analysis only two points were taken into account: none to mild (score 0–2) and severe to necrosis (score 3–4). Also, for the scoring of tumour response only two points were used: no regression or partial regression (score 3–1) and complete tumour regression (score 0). For the tumour dose, the target absorbed dose at the mid-line was quoted (ICRU, 1978). The higher doses outside the target volume were quoted for skin and intestinal reactions. The effects of neutron irradiations were compared with tumour and normal tissue reactions after megavoltage photon therapy.

This treatment was given with a ^{60}Co unit for T_{4B} bladder tumours. As can be seen in Fig. 1, the depth-dose distribution of these γ rays at 80 cm SSD is only slightly better than for a d+T neutron source. Sixty-one patients were irradiated with two parallel-opposed beams in 1967 and 1968 and mid-line doses of 50 to 59 Gy were administered in 20 fractions over four weeks. The data from a later period were also used for further comparisons. In 1974 and 1975 41 patients were irradiated with 8 MV X rays from a Philips SL 75 linear accelerator. A dose of 50 Gy was delivered in 20 fractions over four weeks. As the depth-dose distribution is better than for the neutron generator (Fig. 1), a homogeneous dose distribution could be achieved when only two beams were applied.

The data for all three series of patients were used to estimate RBE values for control of bladder tumour, skin damage and intestinal damage. For the statistical analysis the logistic model (Cox, 1970) was used, describing the relationship between dose

D and probability P of tumour control or serious complications by the formula:

$$P = \exp(a+bD)/(1+\exp(a+bD)).$$

The parameters a and b were estimated from the data, using the maximum likelihood method (Cox, 1970). The adequacy of the model was tested in two ways: firstly a quadratic term in D was added in the exponent and secondly D was replaced by log D, with or without a quadratic term in log D. Neither change resulted in a significant improvement of the fit of the model to the observed data as judged by the likelihood criterion. A dose-independent RBE for neutrons relative to photons only exists if the parameter a for neutron (a_N) equals a for photons (a_{Ph}) This was tested by the likelihood ratio criterion. If so, the RBE can be estimated from b_N/b_{Ph}. From the variances and covariances of b_N and b_{Ph} estimated by the maximum likelihood method an approximate 95% confidence interval for the RBE can be calculated.

RESULTS

It has already been shown (Battermann and Breuer, 1980) that fast-neutron irradiation can be effective in the treatment of inoperable bladder and rectal cancers. However, it has to be stated that in the period of pilot studies high dosages were used (often above 20 Gy) which have led to about 25% severe complications. These complications were caused by overdosing parts of the small and large bowel and the skin. As a result of the poor beam characteristics the determining factor was the AP diameter of the patient. No correlation was found with unfavourable factors like the number of previous laparotomies, hypertension or age, described as predisposing factors for intestinal complications after X-ray therapy (Potish, 1980). Also it was found that neither the number of fractions nor the overall time in our small series of patients influenced the tumour control rate or the complication rate. Of all neutron treated patients, 38 received the dose in 20 fractions over 26–28 days and 28 received the same dose in 25 fractions over 33–35 days.

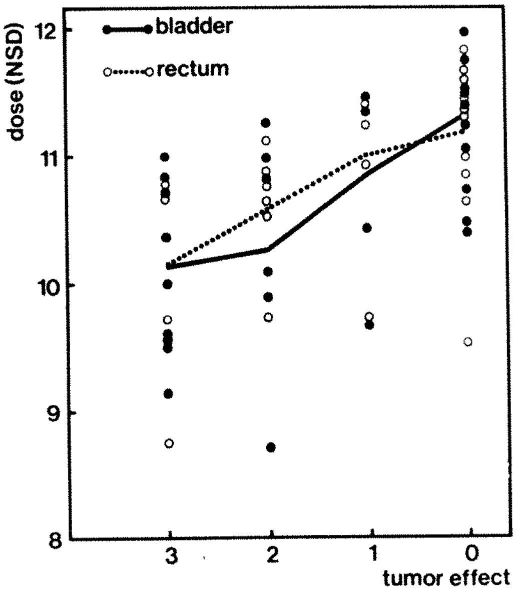


FIG. 3.

Dose-effect relationship for tumour control after neutron irradiation of advanced bladder and rectal tumours.

The scoring system listed in Table I for tumour control was used to describe the dose-tumour effect after fast neutron irradiation for both bladder and rectal cancer. The results are given in Fig. 3. The dose in this figure is total dose, converted into NSD values by the use of the expression $D = \text{NSD} \times N^{0.08} \times T^{0.11}$. In this expression D is the total dose, N the number of fractions and T the overall time (Field, 1972). As can be seen in Fig. 3, no significant difference could be found in the dose-effect relation between bladder and rectal tumours.

Results from earlier treatments with ^{60}Co γ rays and8 MV X rays were used for comparison with the present neutron data. Although the series are small and the effects on tumour, skin and gut had to be scored retrospectively, enough data became available for statistical analysis by the logistic model to give estimations of RBE values for control of bladder tumour, skin damage and gut damage (Table II). In Fig. 4 the resulting dose-effect curves for tumour control after neutron and photon therapy are given, showing a steep shape. For skin and intestinal damage similar curves were found. In our neutron-treated patients hardly any skin sparing effect was noticed. This was demonstrated by covering part of the skin with bolus material during treatment. No difference in skin reaction was noticed compared with the uncovered part of the skin. This can be explained by considering the charged secondaries with relatively high LET and RBE which increase just below the surface much more rapidly than electrons and energetic photons of low LET (Mijnheer *et al.*, 1978). Skin damage might also be due to radiation effects on subcutaneous fat as the kerma for fat is high (Bewley, 1970). The skin and subcutaneous-tissue damage resulted in various degrees of fibrosis and even in radiation-induced ulceration in some patients. The RBE for skin and subcutaneous-tissue damage was 2.94 (2.75–3.13) relative to ^{60}Co γ rays. Intestinal damage was observed in both the small

TABLE II

ESTIMATED PARAMETERS IN THE LOGISTIC MODEL AND RBE WITH 95% CONFIDENCE INTERVAL

	Photons		Neutrons		$a_{Ph} = a_N$				95% confidence interval
	a_{Ph}	b_{Ph}	a_N	b_N	a	b_{Ph}	b_N	RBE	
Serious skin damage	−23.9	0.36	−13.3	0.59	−17.8	0.269	0.790	2.94	2.75–3.13
Serious gut damage	−27.6	0.41	−12.5	0.59	−17.3	0.251	0.796	3.17	2.92–3.42
Bladder tumour control	−8.3	0.13	−9.0	0.45	−8.9	0.140	0.446	3.19	2.73–3.65

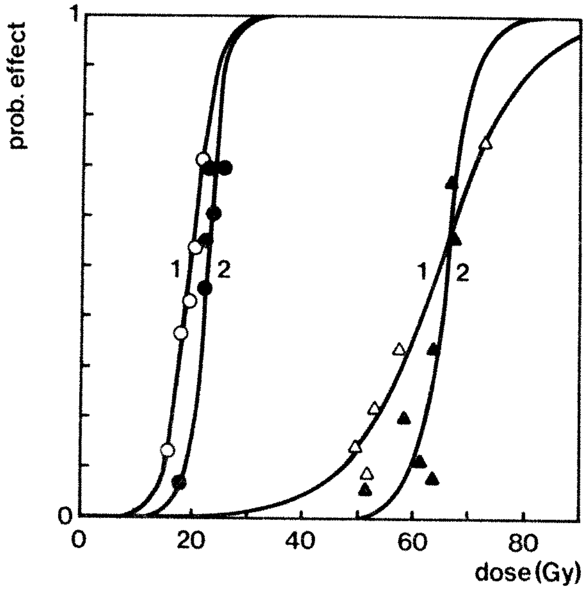


FIG. 4.

Dose-effect relationship for tumour control (1) and for skin and intestinal damage (2) after neutron and photon irradiation for T_{4B} bladder tumours. Neutrons at left, photons at right. As the curves for skin and for intestinal damage happened to be almost identical, just one curve is shown. The points indicate the observed values used to derive the curves.

bowel and the rectosigmoid colon. Patients who died of intestinal complications showed necrosis, fistula and perforation in irradiated parts of the gut at post-mortem examination. Other parts of the intestine were fibrotic with attachment of loops, thus causing impaired mobility of the bowel or even complete obstruction. From the analysed data an RBE of 3.17 (2.92–3.42) for intestinal damage was obtained. However, in the photon-irradiated series of patients no fatal bowel complications were noticed. The RBE for control of bladder tumour was found to be 3.19 (2.73–3.65) relative to ^{60}Co γ rays.

DISCUSSION

Steep dose-response curves are demonstrated for tumour control and for normal-tissue damage after fast neutron irradiation for pelvic tumours. A similar effect was described in the literature after megavoltage X-ray treatment for bladder tumours (Morrison, 1975). However, data from other centres (Cummings, 1978; Stevens *et al.*, 1976) and from this institute (Tierie, 1978) show that local tumour control is hardly ever achieved in inoperable rectal cancer after high-energy photon irradiation. Also, local recurrences after anterior exenteration are resistant to X-ray therapy and the same holds for T_{4B} bladder tumours (Rider and Evans, 1976).

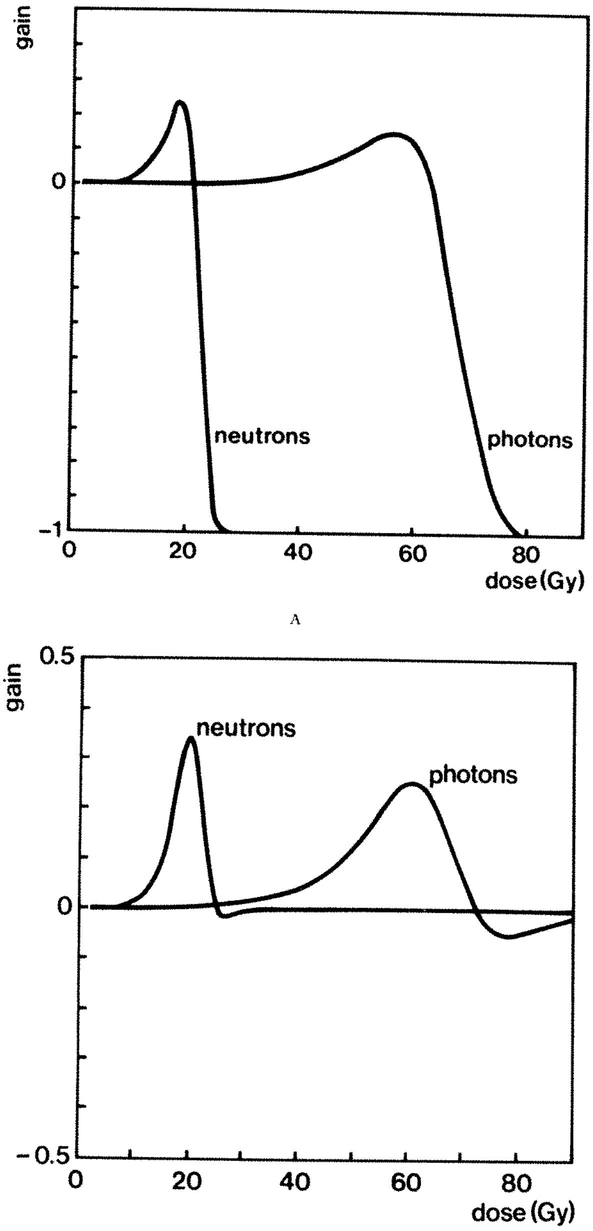
Of course only small numbers of patients were irradiated, both in the neutron group and in the previously treated photon groups. With this restriction it can be said that fast-neutron therapy was superior to high-energy photons in local control of pelvic tumours. According to the information from this pilot study it would be unethical to continue with high-dose neutron irradiation using only two fields. With a six-field technique a more homogeneous dose distribution can be achieved and overdosages avoided. In more than 50 patients treated since 1978 with this technique no fatal complications have been noticed. As no optimal dosage can yet be given for neutron therapy it might be advantageous to use two dose levels in the neutron arm of a clinical trial. The possible advantages of the use of two dose levels in controlled clinical trials have been discussed elsewhere (Breur and Battermann, 1979; Fowler, 1979).

In Fig. 5A and B the therapeutic gain for both neutron and photon therapy is shown graphically, using the equation:

$$\text{gain} = \text{probability of tumour control} - \text{probability of skin damage} \times \text{C1} - \text{probability of gut damage} \times \text{C2}.$$

In this equation C1 and C2 are weighting factors which indicate the severity of skin (C1) and intestinal (C2) damage.

By considering the percentage of local recurrences as serious as the percentage of complications (C1 = C2 = 1) at a certain dose (Fig. 4), it can be learned from Fig. 5A that some gain can be achieved for neutrons in a limited dose range with an optimum at about 19 Gy. The same holds for photon therapy with an optimum at about 56 Gy. If local recurrence is taken to be twice as serious as complications (C1 = C2 = 0.5), the optimum doses are 20 Gy and 60 Gy respectively (Fig. 5B).



A

B

FIG. 5.

Graphical expression of the gain, achieved with neutrons and photons, using the equation: gain = probability of tumour control − probability of skin damage × C1 − probability of gut damage × C2. (A) C1 = C2 = 1, (B) C1 = C2 = 0.5.

In previous studies no severe complications were noticed with X-ray therapy of 50 Gy over four weeks. So the use of two dose levels in the photon arm of a trial could also be advocated.

In May 1978 a controlled clinical trial for bladder and rectal cancer was started. Two dose levels were chosen in the neutron arm, 17 Gy and 19 Gy in 20 fractions over four weeks. The results of this study indicate that an optimum dose will be reached at about 19 Gy, with 50% local tumour control. It can be expected that about 10% severe complications will be seen with this high-dose regime. As all these tumours are incurable by other treatment modalities, a complication rate of 10% is perhaps acceptable.

As various tumours with different characteristics are treated by neutrons, a therapeutic gain will only accrue in a proportion. At present only volume-doubling time and perhaps tumour grade are known as factors that influence radiosensitivity for fast neutrons. Thus a large number of patients in such a mixed group is required to demonstrate the radiobiological advantages (Field, 1976) of neutron irradiation over megavoltage X rays in the treatment of advanced pelvic tumours. It is hoped that the results of clinical trials now in progress at different centres all over the world will lead to a conclusive answer to whether or not fast neutrons should be in the armamentarium of the modern radiotherapist.

To reach a sufficient number of patients in such trials international collaboration will be essential.

REFERENCES

Battermann, J. J. and Breur, K., 1979. Results of fast neutron radiotherapy at Amsterdam. *European Journal of Cancer, Supplement*, 17–22.

1980. Fast neutron irradiation for advanced tumours in the pelvis. *International Journal of Radiation Oncology Biology and Physics* (in press).

Bewley, D. K., 1970. Fast neutron beams for therapy. In *Current Topics in Radiation Research* (North Holland Publishing Co., Amsterdam), p. 249.

Breur, K. and Battermann, J. J., 1979. Clinical trials with fast neutrons in Europe. *European Journal of Cancer, supplement*, 273–277.

Catterall, M. C. and Bewley, D. K., 1979. *Fast Neutrons in the Treatment of Cancer* (Academic Press, New York/London).

Cox, D. R., 1970 Analysis of binary data (Methuen Monographs Series) (Methuen, London).

Cummings, B. J., 1978. Radiation therapy in rectal cancer. *Canadian Journal of Surgery, 21*, 44–56.

Denekamp, J., 1980. Gamma contamination of neutron beams. *British Journal of Radiology, 53*, 819.

Duncan, W. and Arnott, S. J., 1979. Results of clinical applications with fast neutrons in Edinburgh. *European Journal of Cancer, Supplement*, 31–37.

Field, S. B., 1972. The Ellis formulae for X rays and fast neutrons. *British Journal of Radiology*, *45*, 315–317.
1976. An histological survey of radiobiology and radiotherapy with fast neutrons. *Current Topics in Radiation Research Quarterly*, *11*, 1–86.
Fowler, J. F., 1979. Doses and fractionation schemes to be employed in clinical trials of high-LET radiations. *European Journal of Cancer, Supplement*, 263–267.
International Commission on Radiation Units and Measurements, 1978. ICRU Report 29. Dose specification for reporting external beam therapy with photons and electrons (ICRU Publications, PO Box 30165, Washington, DC 20014, USA).
Mijnheer, B. J., Zoetelief, J. and Broerse, J. J., 1978. Build-up and depth-dose characteristics of different fast neutron beams relevant for radiotherapy. *British Journal of Radiology*, *51*, 122–126.
Morrison, R., 1975. The results of treatment of cancer of the bladder. A clinical contribution to radiobiology. *Clinical Radiology*, *26*, 67–75.
Peters, L. J., Hussey, D. H., Fletcher, G. H. and Wharton, J. F., 1979. Second preliminary report of the M. D. Anderson study of neutron therapy for locally advanced gynecological tumours. *European Journal of Cancer, Supplement*, 3–11.
Potish, R. A., 1980. Prediction of radiation related small bowel damage. *Radiology*, *135*, 219–221.
Rider, W. D. and Evans, D. H., 1976. Radiotherapy in the treatment of recurrent bladder cancer. *British Journal of Urology*, *48*, 595.
Stevens, K. R., Allen, C. V. and Fletcher, W. S., 1976. Preoperative radiotherapy for adenocarcinoma of the rectosigmoid. *Cancer*, *37*, 2866–2874.
Tierie, A. H., 1978. Radiotherapy in marginal resectable and non-resectable rectum cancer. *Radiologica Clinica*, *47*, 222–227.
Zoetelief, J., Engels, A. C., Broerse, J. J., Mijnheer, B. J. and Visser, P. A., 1979. Effective measuring point for in-phantom measurements with ion chambers of different sizes *European Journal of Cancer, Supplement*, 169–170.

Book reviews

Diagnostic Radiation: A possible factor in malignancy in patients with chronic inflammatory bowel disease, and other essays. By A. G. Rogers, pp. v + 55, 1980 (Kromar Printing Ltd., Winnipeg, Canada), $7.00.
ISBN 0-919329-01-2

This is a collection of five papers involving assortments of 11 authors, the majority from the University of Manitoba. The foreword indicates that some of these papers have been rejected by conventional journals, but that the authors are so convinced that they have a "message" that they have been prepared to publish them privately (and with high quality printing and presentation).

Basically, a number of case histories are given of patients presenting with adenocarcinomas who had histories of chronic ulcerative colitis, Crohn's disease or similar inflammatory bowel conditions, and who had consequently been subject previously to extensive diagnostic radiation procedures over many years.

From medical records and tables, estimates of the absorbed radiation doses to various organs of interest (in particular the site of the carcinoma) from these procedures have been computed, and in general lie between 30 and 60 rad. The bulk of the dose came from barium enemas, and the authors claim that "counting the number of barium enemas is a valid measure of radiation dosage in most patients with chronic ulcerative colitis".

Probabilities of increased risk per rad for various malignancies have been calculated from the BEIR (1972) report, and compared to the data, which represent of course too small a sample to produce any statistically significant results, but the authors indicate a trend towards an increase in colorectal carcinoma from the diagnostic doses.

Ulcerative colitis is a condition known to predispose to cancer and this will complicate any interpretation. The recent BEIR III (1980)* report now has a section on intestinal and rectal cancers and concludes that a small risk (0.6 excess colon cancer cases per 10^6 person-years per rad) does exist, though it highlights the very wide differences in natural rates between different ethnic populations.

The papers are somewhat anecdotal and repetitive. The authors have been right to point out the risk, but it could have been done in much smaller compass.

J. R. K. Savage.

---

*See page 898.

Cancer Risks by Site. UICC Technical Report Series, Volume 41. Ed. by T. Hirayama, J. A. H. Waterhouse and J. F. Fraumeni, pp. 217, 1980 (International Union Against Cancer, Geneva), 20 Swiss Fr.
ISBN 92-9018-041-2

This is an excellent report which summarizes epidemiological data under selected headings for all the major neoplasms, in order of ICD (9th revision) number. Previously, a useful quick reference book on cancer risks by site has not been available and the only alternative has been an extensive literature search through journals and textbooks. The report is based on a UICC international workshop held in Oslo in October 1976, and the editors are to be congratulated on their efforts.

For each site, the high risk areas and factors are first listed and then five major sections are considered for histology, prognosis, patterns of occurrence, host factors, and environmental factors. Occurrence is subdivided into time trends, international variations, variations within countries, and migration, and the host factors into sex (graphical data provided), age (also graphed, in terms of age-specific incidence rates), genetic predisposition, precancerous lesions, predisposing morbid conditions, and multiple primary neoplasms. There are ten subgroupings under the major heading of environmental factors as follows: socio-economic status, drugs, diet, occupation, sex life and pregnancy, tobacco, alcohol, radiation, air pollution, biological agents.

For many of the possible risk factors the entry is "no information", and the report could have been improved in one respect by the addition of a cross-referenced classified index as well as the existing contents list by cancer site.

For the section on prognosis, age-adjusted five-year survival rates are quoted as a range, for males and for females. However, these ranges are sometimes very wide (*e.g.* salivary glands/female, 59–90%, larynx/male, 43–63%, prostate, 27–53%) and no information is provided as to the centres reporting these results. Also, there is no attempt to quote prognosis as a function of disease stage, even classified only as early or late, for sites such as the cervix uteri.

However, these criticisms are minor ones and do not detract from the great value of this publication which deserves to be found on the library shelves of all radiotherapists, oncologists and epidemiologists. At 20 Swiss Francs it is a bargain.

R. F. Mould.

1981, *British Journal of Radiology*, *54*, 905–907

Technical notes

Measurement of the lumbar spinal canal by diagnostic ultrasound

By Catherine S. Hibbert, Carole Delaygue, Beatrice McGlen and R. W. Porter

Doncaster Royal Infirmary

(*Received March 1981 and in revised form May 1981*)

We have previously reported a method of measuring the spinal canal by ultrasound, and have commented on its clinical significance (Porter *et al.*, 1978). This paper describes in more detail the technique of measurement and its repeatability.

METHOD OF MEASUREMENT

We have used an EMI Diasonograph to measure the spinal canal of over 6000 subjects. The fixed gantry has an advantage in the ease and accuracy of the technique. It is our practice to use a 1.5 MHz transducer, but measurements can be obtained with a 2.5 MHz transducer though with greater attenuation of sound.

The gantry is inclined 15° to the vertical plane, and a B-scan display of the five lumbar vertebrae obtained by scanning the lumbar region a finger's-breadth lateral to the spinous processes. Although Stockdale and Finlay (1980) state that "the identification of the images on the B-scan together with the location of the corresponding echoes on the A-scan is by no means an easy task", we have experienced little difficulty in obtaining a satisfactory B-scan. It may take one or two attempts before the transducer is correctly positioned lateral to the spinous processes, but this is usually achieved without difficulty, and a satisfactory B-scan produced (Fig. 1). The five lumbar vertebrae may not always be displayed together in the same plane if there is a lumbar scoliosis, but this is overcome by rotating the gantry.

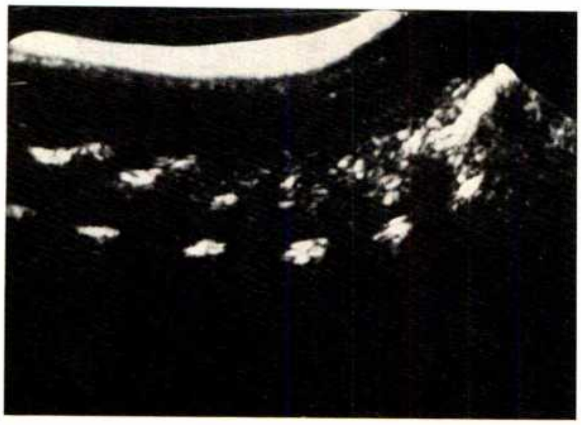


FIG. 1.
B-scan display of lumbar spinal canal.

Each vertebra is first identified on the B-scan before measurements are obtained from the A-scan. Selecting each vertabra in turn, the calipers are first positioned on the B-scan over the echoes believed to be reflected from the canal boundary. The anterior surface of the canal is easily recognized from the distinct echoes of the posterior surface of the vertebral body. It requires more care to position the caliper over the echo from the canal's posterior boundary. It is placed towards the cranial aspect of the laminar echoes. Having positioned the calipers as accurately as possible on the B-scan, actual measurement of the canal is made from the A-scan. In practice, only fine adjustment of the calipers is required for them to be at the apex of the A-scan echoes which are believed to be reflected from the canal's boundary. Large movement of the calipers should now be avoided without referring back to the B-scan to avoid incorrect selection of the A-scan echoes.

The echo from the canal's anterior margin is readily recognized on the A-scan, being the only echo of such large amplitude at this depth. The echo from the posterior canal boundary however is less distinct, being part of a composite echo pattern of reflections from the cranial edge of the lamina where the posterior and anterior surfaces converge (Fig. 2). An echo is sought on the downward slope of this echo complex (Fig. 3).

The transducer is moved slightly in order to maximize the amplitude of the echoes of interest on the A-scan, and when this is achieved, the calipers are adjusted finely to coincide with the apex of these two echoes from the canal boundary. A glance at the B-scan should show the calipers positioned at the boundary of the canal.

We appreciate that correct identification of the echo from the canal's posterior boundary is not easy, and that accuracy of measurement will depend on the ability to display and recognize this echo.

REPEATABILITY

The intraobserver error was measured from 22 patients by the examiner first measuring the five

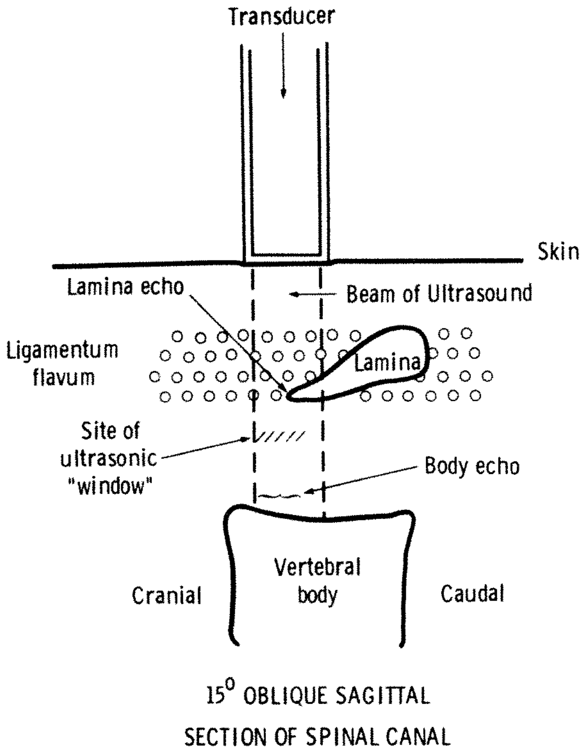


FIG. 2.

Probable origin of echoes from the spinal canal: 15° oblique sagittal section.

lumbar vertebrae as previously described. This was repeated but with another observer recording the measurements from a shielded digital display.

The interobserver error was measured from 100 patients. One examiner measured the five lumbar vertebrae and altered the digital display, and a second examiner who had been out of the room proceeded to measure the canal.

The interobserver error was also recorded between an experienced examiner and a non-medical trainee to determine how long it would take a person new both to the technique and to the concepts of ultrasound to develop a measure of repeatability comparable with that of an experienced examiner.

RESULTS

Table I records the mean and standard deviation of the absolute differences between the two measurements obtained by one examiner. The interobserver error calculated from the absolute difference of the two measurements obtained by two examiners is shown in Table II with a mean error of less than half a millimetre. Table III records the mean interobserver error between an experienced examiner and

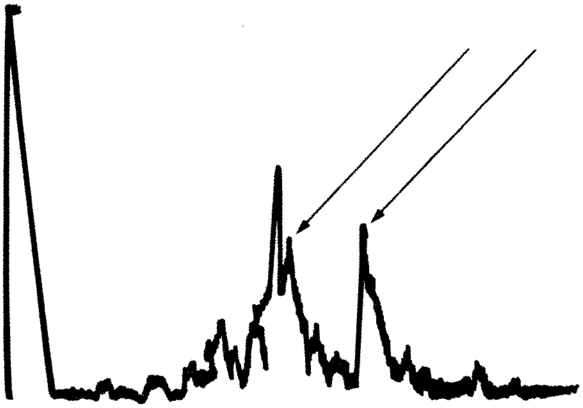


FIG. 3.

A-scan display showing the two echoes to be measured.

TABLE I

MEAN INTRAOBSERVER ERROR FOR 22 PATIENTS

	Mean (cm)	Standard deviation
L1	0.045	0.031
L2	0.044	0.030
L3	0.038	0.030
L4	0.040	0.021
L5	0.041	0.019

TABLE II

MEAN INTEROBSERVER ERROR FOR 100 PATIENTS

	Mean (cm)	Standard deviation
L1	0.038	0.028
L2	0.041	0.030
L3	0.036	0.030
L4	0.037	0.032
L5	0.046	0.037

TABLE III

MEAN INTEROBSERVER ERROR BETWEEN A TRAINEE AND AN EXPERIENCED EXAMINER

	Mean (cm)	Standard deviation
2nd and 3rd week: $n=34$		
L1	0.042	0.037
L2	0.041	0.032
L3	0.052	0.042
L4	0.048	0.040
L5	0.066	0.054
4th and 5th week: $n=36$		
L1	0.038	0.037
L2	0.043	0.044
L3	0.045	0.041
L4	0.050	0.040
L5	0.047	0.043

a trainee in the second and third weeks of training, and also in the fourth and fifth weeks, when a total of 70 patients had been examined.

DISCUSSION

We find a mean repeatability of less than half a millimetre encouraging when attempting to measure a space as complex as the lumbar spinal canal. It is difficult to say exactly what is being measured, but we believe it is some parameter of the central spinal canal in the 15° oblique sagittal plane at the cranial aspect of the lamina. The speed with which a non-medical examiner reached an acceptable degree of proficiency suggests that, with careful tuition, this is not a difficult technique to learn.

REFERENCES

PORTER, R. W., WICKS, M. and OTTEWELL, D., 1978. Measurement of the spinal canal by diagnostic ultrasound. *Journal of Bone and Joint Surgery*, *60-B*, 481–484.

STOCKDALE, H. R. and FINLAY, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101.

A technique for the loading of iridium 192 wire

By L. R. Bridge, M.Sc., D. S. C. Marshall, M.Sc. and W. P. Wilson

Department of Medical Physics, St. William's Hospital, Rochester, Kent, ME1 2NZ

(*Received May 1981*)

Afterloading techniques are increasingly used for interstitial radiotherapy in many centres. These techniques, combined with the use of radium-needle substitutes, provide significant improvements in radiation protection and flexibility of treatment (Morphis, 1960; Henschke *et al.*, 1963; Hall *et al.*, 1966). Approximately half of the hospitals replying to a recent survey (HPA Radiotherapy Physics Topic Group, 1980) have facilities for carrying out iridium-wire implants (Paine, 1972), accessories for which are readily obtainable commercially (Amersham International Limited). The basic technique involves implantation of an array of outer plastic tubes (OPT) which are located at each end by a nylon ball and lead disc. From planning radiographs using dummy marker sources, appropriate lengths of active ^{192}Ir wire are cut and encapsulated into inner plastic tubes (IPT). These are subsequently loaded into the OPT and the lead discs crimped to secure the implant.

Since 1979 we have been replacing the majority of our radium-needle implants by the iridium-wire technique. One problem encountered was that of ensuring, without use of fluoroscopy, that the active wires reproduced the planned geometrical arrangement. The following technique has been developed and provides a simple approach to the problem.

METHOD

The patient leaves the operating theatre with the required arrangement of OPT implanted, located by their nylon balls and uncrimped lead discs. A special set of dummy sources has been constructed consisting of lengths of IPT containing 1 cm lengths of inactive wire. Each centimetre of inactive wire has been encapsulated with a 1 cm space adjacent to it. There is a 1 cm dead end at one end of each of the dummies before the first 1 cm length of wire. Thus each dummy source acts as its own radiographic magnification marker.

In the X-ray room, the loading end of each OPT is decided upon (for accessibility, convenience, etc.) and the disc at the other end is crimped. Dummy sources are introduced from the loading end and pushed into the OPT until the dead end butts up against the crimped disc. The appropriate radiographs are then taken. The crimped (non-loading end) of each OPT is noted on the resulting radiographs. The dead end and length of iridium wire required for each source, to provide the geometry desired by the radiotherapist, is then determined.

Active lengths of ^{192}Ir encapsulated in IPT, with the required dead end, are then made up on a commercial encapsulator (TEM Instruments). These are loaded into the patient in a similar manner to the dummies, so that the dead end butts up against the crimped disc. The remaining discs are then crimped, trapping the IPT (Fig. 1). Figure 2 compares a planning radiograph using the set of dummies with the radiograph of the ^{192}Ir loaded implant.

At the time for removal, sharp long-handled cutters are used by the radiotherapist to sever the OPT between ball and disc at the non-loading end. The ball is removed and the tubes withdrawn from the patient, at the loading end.

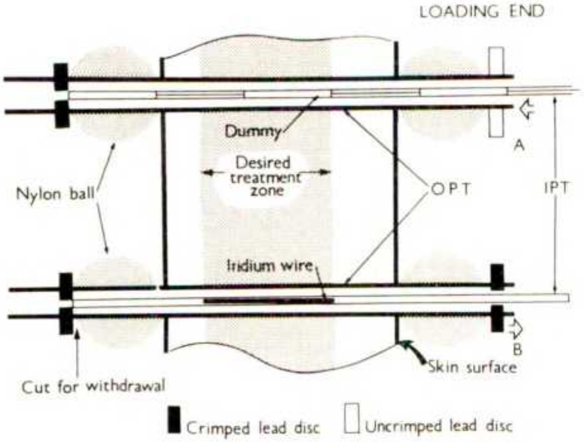


FIG. 1.

Diagram of ^{192}Ir loading method. A, dummy source in position; B, ^{192}Ir wire loaded and secured.

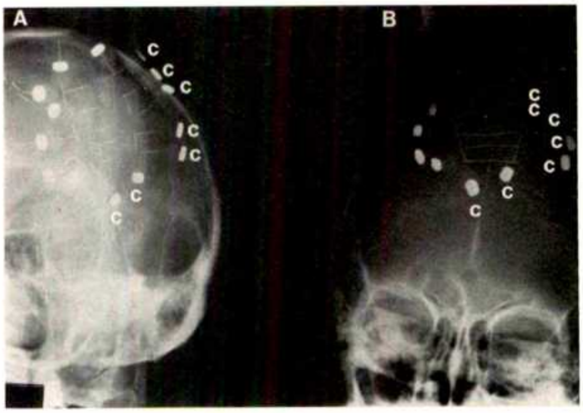


FIG. 2.

A, radiograph with dummies in position; B, radiograph of ^{192}Ir loaded implant. C denotes the crimped ends of the OPT, prior to loading the active wire.

REFERENCES

HALL, E. J., OLIVER, R. and SHEPSTONE, B. J., 1966. Routine dosimetry with tantalum-182 and iridium-192 wires. *Acta Radiologica*, *4*, 155–160.

HENSCHKE, U. K., HILARIS, B. S. and MAHAN, G. D., 1963. Afterloading in interstitial and intracavitary radiation therapy. *American Journal of Roentgenology*, *90*, 386–395.

HPA RADIOTHERAPY PHYSICS TOPIC GROUP, 1980. Radiotherapy equipment and physics services survey 1979/1980 (Hospital Physicists Association, London).

MORPHIS, O. L., 1960. Reduction of radiation hazards to personnel using interstitial implants. *Texas State Journal of Medicine*, January 1960.

PAINE, C. H., 1972. Modern afterloading methods for interstitial radiotherapy. *Clinical Radiology*, *23*, 263–272.

Book review

Choix d'un Système Informatique pour le Calcul des Doses en Radiothérapie. By the Société des Physiciens d'Hôpitaux d'Expression Française, pp. 43, 1980 (S.P.H.E.F. at Institut Curie, 26 Rue d'Ulm, 75231 Paris Cedex 05). Available free of charge on request.

This short French monograph is the report of a working party drawn from members of the French Speaking Hospital Physicists Society (SPHEF) to help members choose a treatment planning system from those available commercially to its members' hospitals. The report is divided into two parts. The first considers general matters such as the comparison of the purpose-built "in-house" mini and the terminal communicating with a remote time-sharing system. It pays attention to the degree of interactivity and to the overall costs to the large and small user.

The second part is a detailed consideration of seven commercial "turnkey" systems and "ISIS", which is an interactive system based on suitable terminals linked by telephone to a time-shared processor in Paris. It is in the form of a tabulated comparison of almost all the relevant factors including hardware, software and price. Most of these comparisons are quantitative and factual. They embody the greater part of all the questions which a would-be purchaser should consider. Subjective comments form no part of the comparison and the user is left to make his own final judgement. With the exception of ISIS all the systems were available internationally, and thus the report is not limited in usefulness to members of SPHEF.

Unfortunately, the comparison must be limited to those systems available at a particular time, in this case January 1, 1980. Attention is drawn to this by the authors and to the fact that the product range is already considerably different. It is hoped that supplements or revisions will be published in the future. Even if the answers to the questions do become out-of-date as the product range evolves, the report will remain useful as drawing attention to the relevant questions in the choice of a treatment planning system; for this reason alone it makes valuable reading.

M. E. ROSENBLOOM.

1981, *British Journal of Radiology*, 54, 909–911

Case reports

The localization of bleeding small bowel lesions for conservative resection: a simple radiographic technique

By *‡J. M. Stevens, M.R.A.C.R., F.R.C.R., †J. M. A. Northover, M.S., F.R.C.S., *M. J. Raphael, M.D., F.R.C.P., F.R.C.R. and †W. W. Slack, Ch.M, F.R.C.S.

Departments of *Radiology and †Surgery, Middlesex Hospital, London W1N 8AA

(*Received May 1981*)

Haemorrhage from the small bowel is a serious diagnostic and therapeutic problem. The value of selective superior mesenteric angiography to localize the source accurately does not require emphasizing; (Athanasoulis *et al.*, 1976; Casarella *et al.*, 1974). However, many of the lesions demonstrated are notoriously difficult to find at operation unless they are actively bleeding at the time (Alfidi *et al.*, 1971; Athanasoulis *et al.*, 1976). We describe a simple method of intra-operative angiography which, because demonstration of the bleeding lesion on the operative films is not an essential requirement, does not involve the use of specialized angiographic equipment. Although only one case is offered to illustrate the method, it seems to possess sufficient versatility to be useful in most situations where intra-operative assistance in isolating a specific loop of small bowel for resection is anticipated.

METHOD

High-quality selective superior mesenteric angiography showing the actual or presumed source of haemorrhage in the small bowel pre-operatively is an essential requirement of the method. Once immediate operative management has been decided upon,

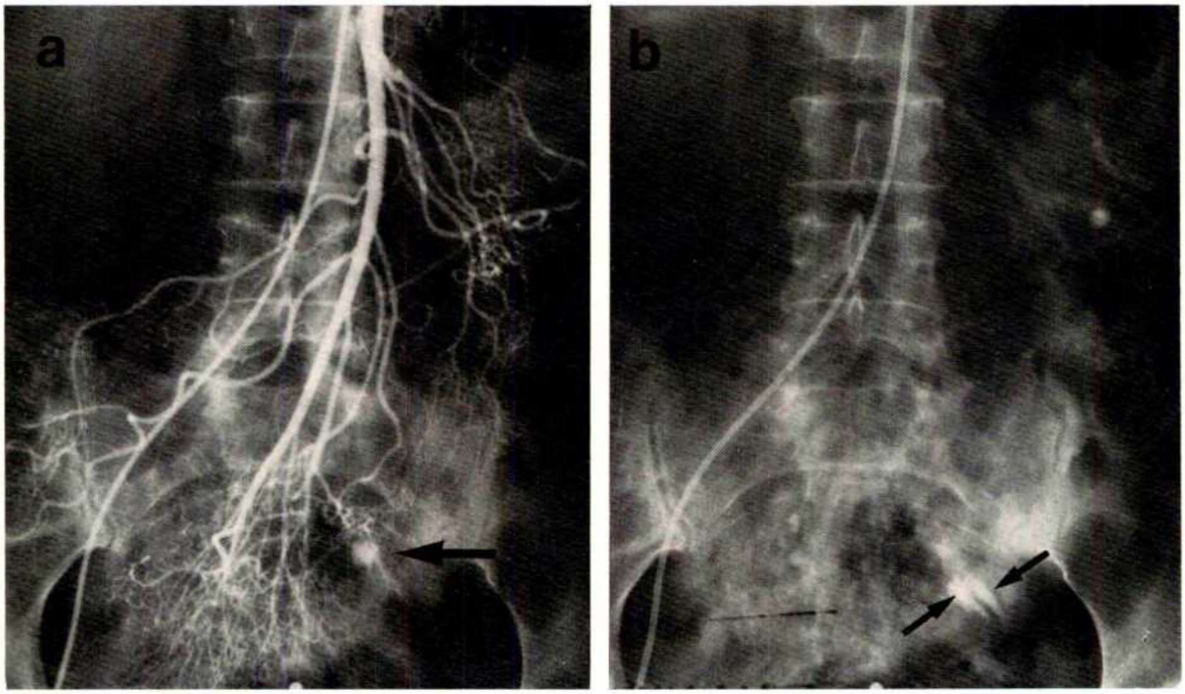


FIG. 1.

Pre-operative selective superior mesenteric arteriogram during active bleeding: (a) arterial phase; (b) venous phase. The large arrow indicates contrast medium collecting in a diverticulum. The two small arrows indicate that contrast medium has left the diverticulum and is lying free in the lumen of the small bowel outlining valvulae conniventes.

---

‡Present address: Department of Diagnostic Radiology, The National Hospital for Nervous Diseases, Queen Square, London W1.

the intra-arterial catheter is left in the superior mesenteric artery (SMA) and the patient transferred from the radiology department to the operating theatre. For this purpose a catheter shape is chosen which will not easily displace from the SMA during transfer, such as a Sidewinder No. 7F (Cordis); it is kept patent in the interval by connection to a continuous arterial drugs infusion set.

A radiologist and radiographer should be present in the operating theatre as well as the necessary surgical staff. The patient is placed on the table over a suitably positioned cassette tunnel of the sort used for operative cholangiography. After the surgeon has opened the abdomen and found blood throughout the small bowel but no obvious bleeding lesion, the bowel is exteriorized on saline-soaked towels and the loops arranged so as to correspond as nearly as possible to their position in the abdomen. A series of sterile metallic numbered markers (available from the radiology department) is sutured to the serosa of the mesentery approximately 5 cm from the mesenteric border of the bowel and 15 cm apart. Mesenteric arteriography is then performed via the catheter; injection of 30 ml of contrast medium (*e.g.* Urografin 76%), using an easily transportable 35 ml Talley syringe operating at a compressed air pressure of 1.5 kg/cm^2, is preferable to a hand injection. A single radiographic exposure is made when nearly all the contrast medium has been delivered from the syringe. A second optional exposure may be made as soon as possible after the first, but is unlikely to be contributory. If a source of haemorrhage happens to be shown at this stage, it can easily be related to the numbered markers. However, it is far more probable that the source will not be seen, and the anatomy of the SMA is then inspected and compared with that displayed by the pre-operative study in which the lesion was shown. By careful scrutiny of the ramifying pattern of the individual branches of the SMA, the artery supplying the bleeding segment should then be identifiable on the intraoperative arteriogram. Thereupon the vessel is easily related to the numbered markers and the appropriate loop of small bowel isolated for resection.

CASE REPORT

A 62-year-old woman was admitted in February 1980 having passed a large melaena stool. Ten, seven and three years previously she had been admitted with a similar history; and on the second occasion, after negative upper and lower gastro-intestinal tract endoscopy, continued haemorrhage led to emergency laparotomy. Extensive small bowel diverticulosis was found with no evidence to locate the actual site of bleeding. A blind resection of 60 cm of proximal jejunum was performed after which she recovered, although a further moderate haemorrhage occurred four years later in 1977.

During this latest admission, the patient suffered repeated episodes of haemorrhage. After negative endoscopy, superior mesenteric angiography demonstrated contrast medium extravasation into the small bowel from a diverticulum (Fig. 1).

Laparotomy and intra-operative angiography were performed using the technique described above. Intra-luminal

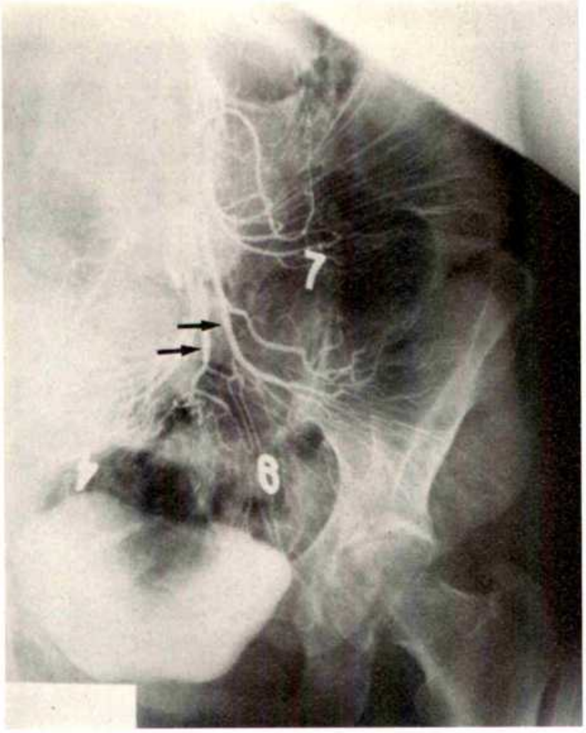


FIG. 2.

Operative arteriogram. The two arrows indicate the arteries identified in the pre-operative angiograms as feeding the bleeding segment of bowel.

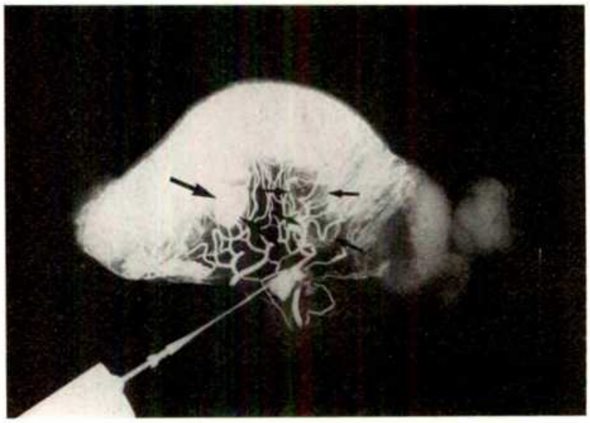


FIG. 3.

Injected specimen. Small arrows indicate unfilled diverticula, large arrows show injectate in a diverticulum.

extravasation could not be seen in the operative films (Fig. 2). On a pre-operative radiograph (Fig. 1) it was evident that the bleeding site was supplied by two parallel vessels which arose opposite the origin of the ileo-colic artery. These vessels appeared on the second intra-operative film (performed after re-arranging the small bowel loops in their approximate anatomical position) in the region of marker 6. Twelve centimetres of small bowel around the location of this marker were resected and the abdomen closed. Specimen radiography (Fig. 3) demonstrated the vasculature of several apparently intact diverticula, while one contained extravasated contrast medium. It was assumed that this had been the site of haemorrhage. Post-operatively the patient made an uneventful recovery and remains well six months later.

Discussion

Of patients with gastro-intestinal haemorrhage who come to angiography for the purpose of diagnosing the bleeding site, some 10% may be expected to show the source in small bowel distal to the ligament of Treitz (Casarella *et al.*, 1974). The commoner lesions found are Meckel's diverticulum (Faris and Whitley, 1973), bleeding jejunal diverticulum (as in our case, also Kittredge *et al.*, 1969; Sos *et al.*, 1978), and arterio-venous fistulae (Casarella *et al.*, 1974). A bleeding small bowel diverticulum or an arterio-venous malformation are the lesions which most often prove impossible to find at laparotomy (Taylor, 1969; Athanasoulis *et al.*, 1976; Davis, 1977), unless they are actively bleeding at the time.

Non-radiographic intra-operative methods of localizing small bowel arterio-venous malformations have been described by Fogler and also by Evans (Fogler and Golembe, 1978; Evans *et al.*, 1978). One involved making an injection of methylene blue into the SMA and observing the wash-out rate of the dye, while the other required sampling of blood from veins within the mesentery draining the suspected loop for blood gas analysis. Both are complex and applicable only to one type of lesion.

Intra-operative angiography was described by Margulis as early as 1960 (Margulis *et al.*, 1960), using a direct injection of contrast into the SMA. It was described again by Alfidi *et al.* (1971) who used a system of mesenteric markers similar to ours. However, their method required that the intra-operative angiogram should show the lesion, and necessitated that operation be performed in the angiographic suite where the necessary specialized equipment was available. This is not a practical proposition in most hospitals.

We feel that our method has decisive advantages over others described. The placement of the angiographic catheter in the SMA via the femoral route pre-operatively avoids direct canalization of the SMA during operation. More importantly, because the method does not require that the actual bleeding lesion be shown in the operative arteriogram, specialized equipment is not required in the operating theatre. This means that the method is more versatile and should be able to localize any type of bleeding lesion in the small bowel at laparotomy, provided of course it has been shown in a high quality pre-operative angiogram.

REFERENCES

Alfidi, R. J., Esselstyn, C. D., Tamar, R., Klein, H. J., Hermann, R. E., Weakley, F. L. and Turnbull, R. B., 1971. Recognition and angio-surgical detection of arterio-venous malformations of the bowel. *Annals of Surgery*, *174*, 573–581.

Athanosoulis, C. A., Waltman, A. C. and Novelline, R. A., 1976. Angiography: its contribution to the emergency management of gastrointestinal haemorrhage. *Radiologic Clinics of North America*, *14*, 265–280.

Casarella, W. J., Galloway, S. J., Taxin, R. N., Follet, D. A., Pollok, E. J. and Seaman, W. B., 1974. Lower gastro-intestinal haemorrhage. New concepts based on arteriography. *American Journal of Roentgenology*, *121*, 357–368.

Davis, G. E., 1977. Multiple small bowel diverticula. *Journal of the Maine Medical Association*, *68*, 79–81.

Evans, W. E., O'Dorisio, T. M., Molnar, W., Martin, E. W., Wooley, C. F. and Cooperman, M., 1978. Intra-operative localisation of intestinal arterio-venous malformation. *Archives of Surgery*, *113*, 410–412.

Faris, H. C. and Whitley, J. E., 1973. Angiographic demonstration of Meckel's diverticulum. Case report and review of the literature. *Radiology*, *108*, 285–286.

Fogler, R. and Golembe, E., 1978. Methylene blue injection: an intra-operative guide in small bowel resection for arterio-venous malformation. *Archives of Surgery*, *113*, 194–195.

Kittredge, R. B., Coliace, W. M., Kanick, W. and Finby, N., 1969. The angiography of haemorrhage. *American Journal of Roentgenology*, *107*, 181–190.

Margulis, A. R., Heinbecker, P. and Bernard, H. R., 1960. Operative mesenteric angiography in the search for the site of bleeding in unexplained gastro-intestinal haemorrhage. *Surgery*, *48*, 534–539.

Sos, P. A., Lee, J. G., Wixson, C. and Sniderman, K. W., 1978. Intermittent bleeding from minute to minute in acute massive gastrointestinal haemorrhage: arteriographic demonstration. *American Journal of Roentgenology*, *131*, 1015–1017.

Taylor, M. T., 1969. Massive haemorrhage from jejunal diverticulosis. *American Journal of Surgery*, *118*, 117–120.

1981, *British Journal of Radiology*, 54, 912–915

Case reports

Therapeutic adrenal venous infarction in ACTH-dependent Cushing's syndrome

By *J. Rosenstock, M.D., †D. Allison, B.Sc., M.D., F.R.C.R., *G. F. Joplin, Ph.D., F.R.C.P.,
‖P. D. Lewis, M.D., M.R.C.P., M.R.C.Path., *K. Mashiter, Ph.D.,
‡R. B. Welbourn, M.A., M.D., F.R.C.S. and *M. C. White, M.R.C.P.

*Endocrine Unit, Department of Medicine; and Departments of †Diagnostic Radiology, ‡Surgery and ‖Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS

(*Received March 1981 and in revised form May 1981*)

Adrenal infarction is a well-recognized complication of diagnostic adrenal phlebography and if it occurs bilaterally it may lead to adrenal insufficiency (Eagan and Page, 1971; Fisher *et al.*, 1971; Taylor and Sachs, 1976). This is because the delicate adrenal veins are easily obstructed and over-distended during the injection of contrast medium, leading to venous rupture and thrombosis with secondary adrenal infarction. Remission of Cushing's syndrome, apparently due to adrenal adenoma, has been reported after diagnostic adrenal phlebography (Fellerman *et al.*, 1970; Jørgensen and Stiris, 1974), and the ectopic ACTH syndrome has been controlled in two reported cases by intentional bilateral venous infarction (Eddy *et al.*, 1973; Rogove *et al.*, 1976).

We report the successful use of adrenal venous infarction in a patient with severe life-threatening ACTH-dependent Cushing's syndrome. The procedure ameliorated the hypercortisolism as a temporary measure in preparation for definitive surgical adrenalectomy.

Case Report

A 26-year-old man was referred to us in October 1979 with extremely severe Cushing's syndrome. Four months previously a diagnosis of hypercortisolism had been made at his local hospital. Adrenal venography had shown an enlarged left adrenal gland but it had been impossible to cannulate the right adrenal vein. A left adrenal carcinoma was suspected and that gland was removed through a mid-line abdominal incision. The histology showed adrenal hyperplasia with no evidence of malignancy. Post-operatively his condition continued to worsen and he became extremely ill with severe hypokalaemia, and greatly elevated plasma cortisol, urinary 17-oxosteroid and 17-hydroxysteroid levels.

On arrival here in October 1979 he was very ill, with a grossly Cushingoid appearance. He had severe proximal muscle weakness and wasting, and was unable to sit up unaided. He had marked conjunctival oedema and his skin was livid with widespread and very marked purple striae and a gaping abdominal wound. The blood pressure was 140/90. There was also dangerous hypokalaemia (initial K^+ 1.6 mEq/l) and diabetes mellitus (initial plasma glucose 15.8 mmol/l). He was immediately started on intravenous potassium replacement.

It was considered that his condition was too grave to tolerate further investigation or operations and that drugs, such as metyrapone, might not act rapidly enough to control his condition. It was therefore decided to try to reduce the cortisol production by inducing venous thrombosis in the remaining right adrenal. The procedure was performed within 24 hours of admission and was covered with hydrocortisone and broad spectrum antibiotics. A Cordis Femorol-Visceral catheter (French 7 gauge) was introduced selectively into the right adrenal vein and a phlebogram showed a greatly enlarged gland (Fig. 1). The catheter was wedged in the vein which was then deliberately ruptured after distension of the adrenal venous system with a mixture of diatrizoate (Urografin 76%) and 50% dextrose solution (Fig. 2). The procedure was uneventful and the patient felt only transient lumbar pain. The urine-free cortisol (measured by the method of Beardwell *et al.*, 1968) decreased from an initial extremely high level of 15360 nmol/24 h (normal <270 nmol/24 h) to 3910 nmol/24 h but soon increased again, so on day 19, metyrapone was started at 2 g/24 h (Table I). Subsequently his general condition and muscle strength showed a definite improvement with some early signs of healing of the abdominal wound, and the fasting plasma glucose and potassium levels became normal.

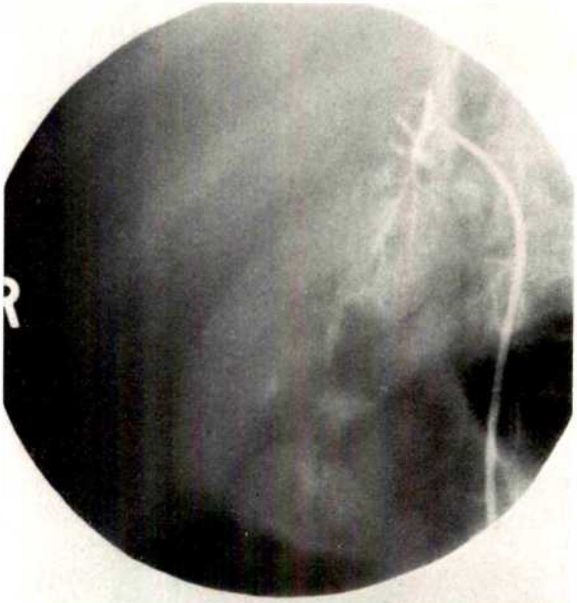


Fig. 1.

Selective right adrenal venogram. A contrast injection into the right adrenal vein shows a generally enlarged gland with no evidence of a localized tumour. The poor technical quality of the study is due to the rapid respiratory rate in a very sick patient.

TABLE I

SERIAL URINE AND SERUM CORTICOIDS

	Days after each infarction	Urine-free cortisol (nmol/24 h)	S. cortisol† 9 a.m. (nmol/l)	Metyrapone dose (g/24 h)
First adrenal infarction	−1	15360	573	nil
	8	3910	—	nil
	12	5247	555	nil
	28	—	606	nil‡
	32*	16349	—	nil‡
	44	—	489	2
Second adrenal infarction	−20*	16349	—	nil
	−1	—	520	2
	4	—	842	nil
	7	—	835	nil
	11	—	244	2
	14	3492	641	nil
	21	352	439	1
	24	—	335	1
	28	274	385	1
	32	—	274	1

*The same day.

†Serum cortisol levels have been corrected for the contribution from compound S, since this was measured separately.

‡Metyrapone temporarily discontinued.

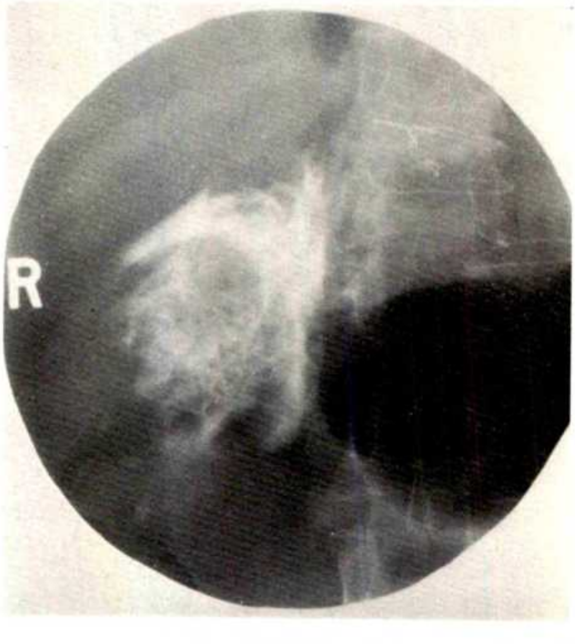


FIG. 2.

Post-infarction radiograph of right adrenal gland. Extravasated contrast medium is seen lying in the retroperitoneal space in the region of the right adrenal gland. The appearances are due to adrenal vein rupture following a deliberate pressure injection through a wedged catheter.

Results of the initial endocrine investigations then became available; they revealed raised ACTH levels (measured by the method of Rees *et al.* (1971)) in the range of 102–359 ng/l (normal < 10 to 80 ng/l), indicating that his condition was either pituitary-dependent or due to an ectopic ACTH-producing tumour. The functional tests gave ambiguous results: the urine-free cortisol was not suppressed by 8 mg/day of dexamethasone for two days, while the urinary 17-OGS rose from 167 to 509 μmol/24 h in response to a metyrapone test using 750 mg 4-hourly for six doses. There was no obvious pituitary tumour on skull tomography, nor could a tumour be found radiologically in the lungs, thymus or thyroid.

As no definitive diagnosis could be made on functional testing, and the Cushing's syndrome was again advancing despite the metyrapone treatment, it was decided to perform multiple venous sampling for ACTH levels in order to locate a source of ectopic ACTH production (Corrigan *et al.*, 1977). Blood was taken from the jugular, thyroid and azygos veins, both venae cavae, hepatic veins, left adrenal vein and from the right adrenal vein which was seen to be still draining some remaining glandular tissue. After the sampling, a second venous infarction was performed. Again there was transient lumbar pain but no other complication. All the samples showed similar values of ACTH (about 270 ng/l) and no "hot spot" or significant difference from the simultaneous peripheral venous samples was found.

Seven days after the second adrenal infarction the patient was restarted with his previous dose of metyrapone, but this time, on the 5th day of treatment, he developed symptoms suggestive of an Addisonian crisis, which resolved on stopping the drug. Subsequently metyrapone was restarted at the lower dose of 1 g/day. Thereafter his condition improved dramatically with complete healing of the abdominal wound, increasing muscle strength and resolution of the diabetes and electrolyte disturbances. Biochemically the hypercortisolism became less, reaching almost normal values for urine-free cortisol.

On January 21, 1980 he was considered fit enough for operation and a right adrenalectomy was undertaken by the lateral route (Welbourn, 1977). The tenth rib was resected and an incision was made through the diaphragm over the gland. The adrenal appeared very large and was the same colour as the kidney. It was firmly adherent to the inferior vena cava, so that its excision was difficult. It was, however, removed in one piece. The weight of the gland was 32 g (Fig. 3) and the histology showed adrenal hyperplasia with extensive zones of necrosis and haemorrhage (Fig. 4). The patient made an uneventful recovery and the wound healed

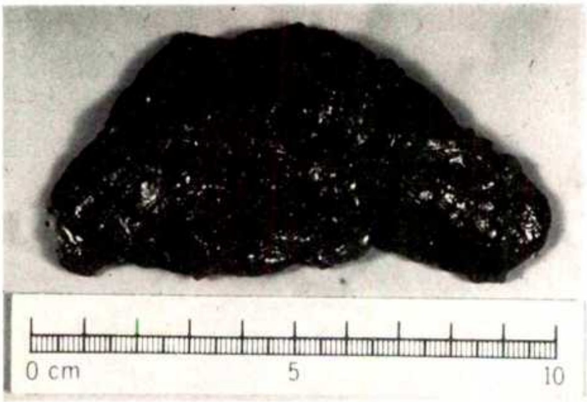


FIG. 3.

Gross appearance of infarcted right adrenal. Haemorrhagic swelling and necrosis is evident, with normal gross morphology only in isolated areas along lower border.

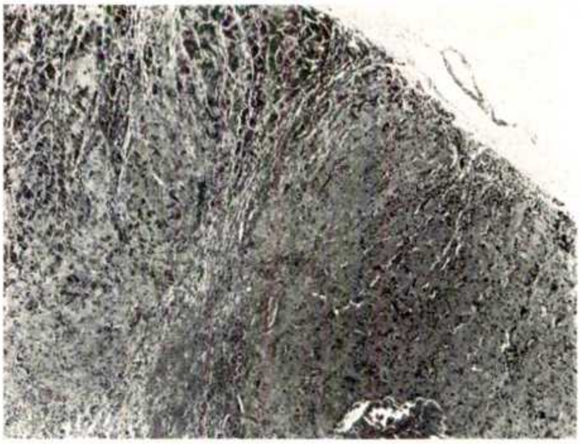


FIG. 4.

The adrenal cortex shows extensive haemorrhagic infarction. Viable adrenal cortical cells are present to the left of the field shown, while gross haemorrhage is seen in two areas in the lower half of the field. Haematoxylin-eosin. × 30.

quickly. He was discharged fit and well seven days after operation on hydrocortisone 20 mg/24 h. His blood pressure had fallen to 120/70, and the GTT was normal.

DISCUSSION

This report illustrates some of the difficulties of managing patients with severe Cushing's syndrome. Metyrapone is a useful drug in lowering cortisol production by a selective inhibition of 11β-hydroxylase and we find that the clinical response is usually rapid. However, some patients take longer to be controlled this way, as there is variation in the sensitivity to the drug (Jeffcoate *et al.*, 1977). We considered metyrapone for the initial treatment to control the hypercortisolism, but, in view of the patient's desperate state, it was thought that infarction of his single adrenal might be the most rapid and certain way to obtain control. If successful, it might also allow time for further investigation and planning of definitive treatment. The procedure was performed twice with obvious benefit, as shown by the impressive clinical improvement and reduction of cortisol output. After the second infarction he was easily controlled by a low dose of metyrapone.

Adrenal venography is generally considered to be a low risk procedure but is nevertheless one of the most invasive of available diagnostic vascular investigations. Lecky *et al.* (1976) made an extensive review of the literature. They surveyed reports of 431 angiographic studies made for adrenal disorders including Cushing's syndrome, Conn's syndrome, virilizing syndromes and carcinoma. They found 39 complications (9%) which were divided into 34 cases (8%) with transient complications (flank pain, adrenal vein thrombosis, extravasation of contrast material or haematoma formation) and five cases (1%) of permanent complications (three adrenal insufficiency, one remission of Cushing's and one remission of Conn's syndrome). No deaths occurred.

This complication of inadvertent adrenal ablation during diagnostic phlebography has been turned to therapeutic advantage by the deliberate induction of adrenal insufficiency in patients with metastatic carcinoma of the breast (Lecky and Plotkin, 1971; Zimmerman *et al.*, 1974; Jablonsky *et al.*, 1977). Of particular interest are those reports of remission of Cushing's syndrome after adrenal venography in two patients with probable adrenal adenoma (Fellerman *et al.*, 1970; Jørgensen and Stiris, 1974). Intentional bilateral adrenal ablation by venous infarction has also been successfully achieved, and led to control in two cases of ectopic ACTH syndrome, where bilateral adrenalectomy was contraindicated: one patient had metastatic carcinoma of the prostate producing ACTH (Eddy *et al.*, 1973) and the other a metastatic medullary carcinoma of the thyroid (Rogove *et al.*, 1976). The application of a therapeutic vascular technique to the venous system in this way is an interesting extension of the use of interventional radiological procedures in endocrine disease; therapeutic arterial embolization is now well established as a valuable measure for controlling the excessive hormone production of endocrine tumours of the pancreas and liver (Allison, 1978).

We conclude by suggesting that adrenal infarction might be regarded as an alternative to bilateral adrenalectomy as a form of palliation in patients with

1981, *British Journal of Radiology*, *54*, 915–918 OCTOBER 1981

ectopic ACTH syndrome due to advanced malignancy. This approach also appears valuable in end-stage Cushing's syndrome where it is essential to gain at least a temporary metabolic control to prepare the patient for adrenal operation when adrenolytic drug control is inadequate.

ACKNOWLEDGMENTS

D. J. A. wishes to express his gratitude to Cordis UK Ltd. for their kind support.

J. R. gratefully acknowledges support from the British Council and the Social Security System of Costa Rica.

We are pleased to acknowledge the skilled help of the Nursing Staff of the Metabolic Unit in the care and monitoring of this patient's condition, and Professor Lesley H. Rees for the ACTH assays.

REFERENCES

ALLISON, D. J., 1978. Therapeutic embolization. *British Journal of Hospital Medicine*, *20*, 707–715.

BEARDWELL, C. G., BURKE, C. W. and COPE, C. L., 1968. Urine free cortisol measured by competitive protein binding. *Journal of Endocrinology*, *42*, 78–89.

CORRIGAN, D. F., SCHAAF, M., WHALEY, R. A., CZERWINSKY, C. L. and EARLL, J. M., 1977. Selective venous sampling to differentiate ectopic ACTH secretion from pituitary Cushing's syndrome. *New England Journal of Medicine*, *296*, 861–862.

EAGAN, R. T. and PAGE, M. I., 1971. Adrenal insufficiency following bilateral adrenal venography. *Journal of the American Medical Association*, *215*, 115–116.

EDDY, R. L., MCMURRAY, J. F. JR., BEST, E. B., HENDERSON, B. W. and SMITH, V. T., 1973. Adrenal ablation by venous catheter. *Annals of Internal Medicine*, *79*, 273–274.

FELLERMAN, H., DALAKOS, T. G., and STREETEN, D. H. P., 1970. Remission of Cushing's syndrome after unilateral adrenal phlebography. Apparent destruction of adrenal adenoma. *Annals of Internal Medicine*, *73*, 585–589.

FISCHER, C. E., TURNER, F. A. and HORTON, R., 1971. Remission of primary hyperaldosteronism after adrenal venography. *The New England Journal of Medicine*, *285*, 334–336.

JABLONSKY, R. D., MEANEY, T. F. and SCHUMACHER, O. P., 1977. Transcatheter adrenal ablation for metastatic carcinoma of the breast. *Cleveland Clinic Quarterly*, *44*, 57–63.

JEFFCOATE, W. J., REES, L. H., TOMLIN, S., JONES, A. E., EDWARDS, C. R. W. and BESSER, G. M., 1977. Metyrapone in long-term management of Cushing's disease. *British Medical Journal*, *ii*, 215–217.

JØRGENSEN, H. and STIRIS, G., 1974. Hypertensive crisis followed by adrenocortical insufficiency after unilateral adrenal phlebography in a patient with Cushing's syndrome. *Acta Medica Scandinavica*, *196*, 141–143.

LECKY, J. W. and PLOTKIN, D., 1971. Adrenal function ablation utilizing the angiographic catheter. *Journal of the American Medical Association*, *218*, 1438.

LECKY, J. W., WOLFMAN, N. T. and MODIE, C. W., 1976. Current concepts of adrenal angiography. *Radiological Clinics of North America*, *19*, 309–352.

REES, L. H., COOK, D. M., KENDALL, J. W., ALLEN, C. F., KRAMER, R. M., RATCLIFFE, J. G. and KNIGHT, R. A., 1971. A radioimmunoassay for plasma ACTH. *Endocrinology*, *89*, 254–261.

ROGOVE, H. J., MEANEY, T. F., SCHUMACHER, O. P. and BRAVO, E. L., 1976. Cushing's syndrome successfully treated by transcatheter adrenal ablation. *Clinical Research*, *24*, 10A.

TAYLOR, H. C. and SACHS, C. R., 1976. Primary aldosteronism: remission and development of adrenal insufficiency after adrenal venography. *Annals of Internal Medicine*, *85*, 207–209.

WELBOURN, R. B., 1977. Surgery of the adrenal glands. In *Operative Surgery—Abdomen*, 3rd edit. (Butterworths, London), pp. 403–419.

ZIMMERMAN, C. E., EISEMBERG, H., SPARK, R. and ROSOFF, C. B., 1974. Transvenous adrenal destruction: clinical trials in patients with metastatic malignancy. *Surgery*, *75*, 550–556.

Lymphography in post-vagotomy chylous ascites

By *A. Schulman, F.R.C.R., M.R.C.P., †I. N. Marks, F.R.C.P., ‡D. M. Dent, Ch.M., F.R.C.S., F.C.S. (S.A.) and †A. H. Girdwood, M.R.C.P.

*Department of Radiology, †Gastrointestinal Clinic and ‡Department of Surgery, Groote Schuur Hospital and University of Cape Town, South Africa.

(*Received February 1981*)

Chylous ascites is a rare complication of abdominal operation, caused by damage to the cisterna chyli or its chyle-carrying anterior tributaries from the small intestine. To our knowledge, this is the first case in which lymphography has established the diagnosis of cisterna chyli obstruction in this situation.

CASE REPORT

A 72-year-old woman with chronic obstructive lung disease and a history of moderate alcohol intake had suffered for ten years from an intractable duodenal ulcer which had failed to respond satisfactorily to antacids and cimetidine. Recently the pain had worsened, there was frequent vomiting, and a giant duodenal ulcer was shown radiologically and endoscopically. Truncal vagotomy and gastroenterostomy were performed. On the ninth post-operative day, milky fluid began to drain from the operative drain site but this settled after two days, and she was discharged. She was referred to us one month post-operatively with symptoms of gradually increasing abdominal swelling, ankle oedema and pale, offensive faeces. Her ascites was aspirated, revealing chylous fluid with a triglyceride content three times that of serum, and the faecal fat content was raised (23.4 m mol/day).

Bipedal lymphography showed evidence of partial obstruction at the level of the cisterna chyli. Rate of flow up the iliac and para-aortic lymphatics was abnormally slow and there was some retrograde flow anteriorly into mesenteric lymphatics and laterally into retroperitoneal lymphatics

---

Address for reprints Dr. A. Schulman, Department of Diagnostic Radiology, Tygerberg Hospital, Parowvallei, Cape, South Africa.

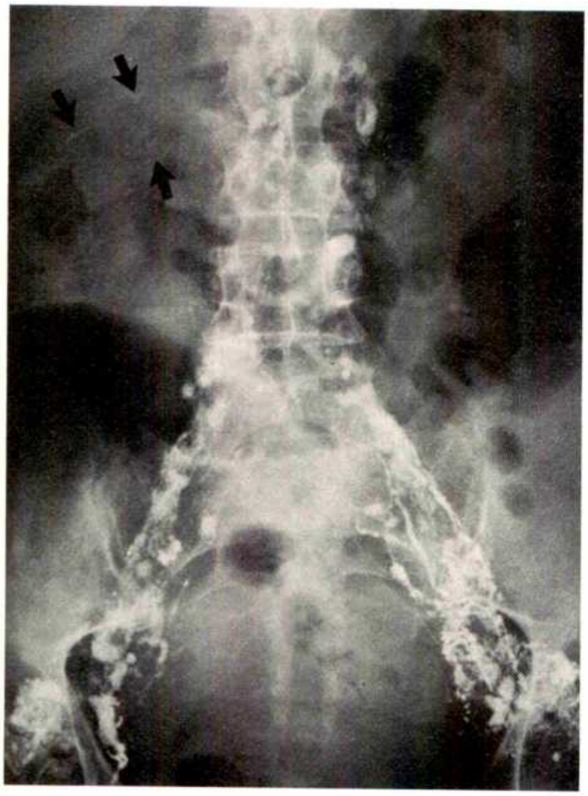


FIG. 1.

Five hours after the completion of the bipedal infusion, the iliac and para-aortic lymphatics remain distended with contrast medium. Lateral retroperitoneal lymphatics have filled (arrows).

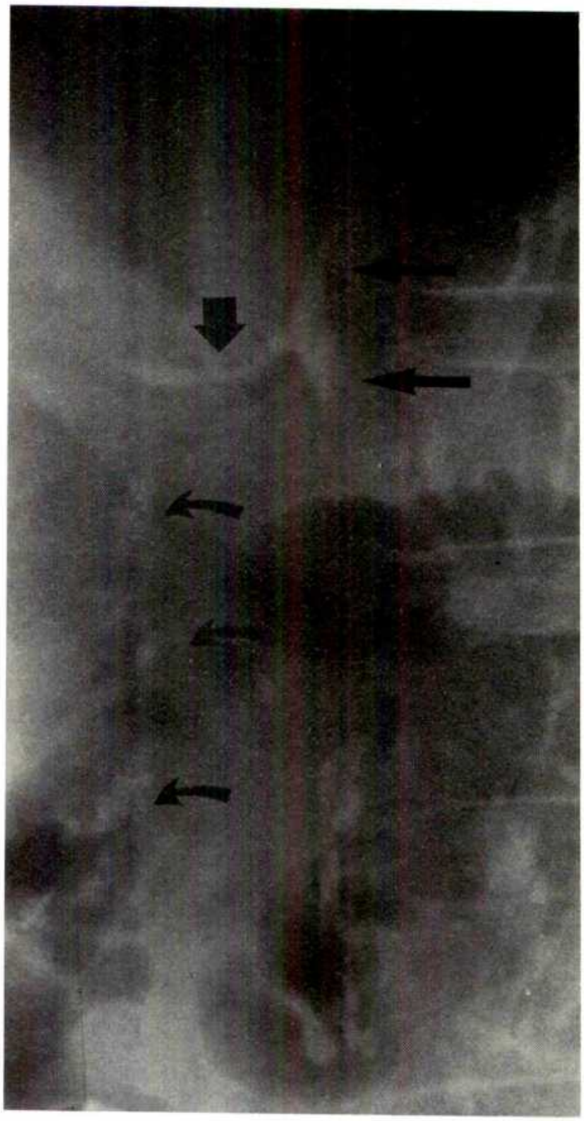


FIG. 2.

Lateral radiograph shows the distended cisterna chyli (long arrows) with contrast medium passing in a retrograde manner into an anterior visceral lymphatic (short arrow). Other mesenteric nodes lying well anterior to the spine have also begun to fill (curved arrows).

(Fig. 1). The cisterna chyli was well distended, with an anterior lymphatic filling in a retrograde manner directly from it (Fig. 2). Some contrast medium passed slowly into the thoracic duct which was thinly and sparsely opacified. Two days later, contrast medium could be seen lying free in the peritoneal cavity (Fig. 3). The small bowel appeared normal on barium study but peroral capsule biopsy showed dilated lymphatics within the villi.

She was treated with diuretics and intravenous hyperalimentation but the ascites nevertheless required aspiration and her nutritional state deteriorated. At a second laparotomy three-and-a-half months after the first, the upper abdomen was found to be involved by dense adhesions preventing definitive dissection at the site; a LeVeen shunt was placed from the pelvic peritoneal cavity to the right internal jugular vein. She continued to deteriorate however and died three weeks later after developing pneumonia complicating her chronic obstructive lung disease.

Post-mortem examination showed a benign peptic ulcer in the duodenal bulb. Dense upper abdominal adhesions were present, preventing adequate demonstration of the cisterna chyli at this site. There was no other intra-abdominal pathology.

DISCUSSION

The English literature mentions 11 cases of chylous ascites following retroperitoneal lymphadenectomy (Ross *et al.*, 1971; Bigley and Chenault, 1975; Spence *et al.*, 1977; Herz *et al.*, 1978; Miedema *et al.*, 1978), two following operations for abdominal aortic aneurysm (Bradham *et al.*, 1970; Klippel and Hardy, 1971), one each following pancreaticoduodenectomy (Walker, 1967), bilateral coeliac ganglionectomy (Ikard, 1972) and removal of left paravertebral, pararenal neuroblastoma (Roy *et al.*, 1970), four following venous shunts for portal

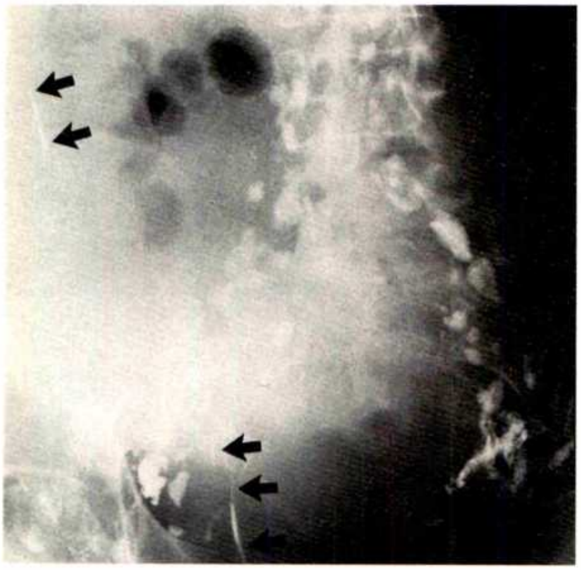


FIG. 3.

Two days later, a right decubitus radiograph shows contrast medium lying free in the peritoneal cavity (arrows). The medium descended to the left side when the patient lay on that side (not illustrated).

hypertension (Klippel and Hardy, 1971; Boyd and Wooldridge, 1955; Maywood *et al.*, 1978; Freund *et al.*, 1979) and four following truncal vagotomy (Cox *et al.*, 1966; Clain, 1971; Musgrove, 1972; Hocking and Barth, 1978). There is therefore a special risk of chylous ascites after certain types of operation.

As the cisterna chyli is a para-aortic retroperitoneal structure, it is not surprising that the various forms of retroperitoneal dissection in the above list account for the majority of cases; in one of them (Ross *et al.*, 1971), lymphography showed the approximate site of laceration and direct leakage.

In portal hypertension, there is an increased flow of lymph from the viscera due to the venous stasis and the raised pressure transmitted via the lymphovenous communications. This facilitates significant chylous leak from the inevitable lymphatic tears occurring during the various shunt operations for portal hypertension. Clinically significant and persistent chylous ascites has followed splenorenal shunt (Maywood *et al.*, 1978; Freund *et al.*, 1979; Warren, 1978), inferior mesenteric-left renal shunt (Boyd and Wooldridge, 1955) and superior mesenteric-inferior vena cava shunt (Klippel and Hardy, 1971). In a case following splenorenal venous shunt (Maywood *et al.*, 1978), lymphography was normal, which is not surprising as the lacerated lymphatic would have been lateral to the cisterna chyli "main line".

In two cases of chylous ascites following truncal vagotomy, the cause was a torn lymphatic vessel in the region of the vagotomy procedure, close to the gastro-oesophageal junction; this was established at re-operation (Clain, 1971; Musgrove, 1972). In a third case, the leaking lymphatic lay adjacent to the left gastric pedicle which had been divided during re-vagotomy (Hocking and Barth, 1978). This was controlled at a third operation by a transfixion suture. The fourth case settled conservatively (Cox *et al.*, 1966) and it was here suggested that, during surgical division of the posterior vagal trunk, interference with the cisterna chyli had resulted in obstruction. This seems to have been the cause in our patient. The posterior vagal trunk is related to the back of the oesophagus as it traverses its diaphragmatic hiatus, which in turn lies anterior, cephaled and slightly to the left of the aortic hiatus through which the cisterna chyli passes (Warwick and Williams, 1973).

Bipedal lymphography is a reliable method of showing the "main line" of lymphatic drainage via cisterna chyli and thoracic duct. It can be used therefore to localize laceration of these trunks and demonstrate direct spill of chyle or, as in this case, obstruction causing backward flow and delayed seepage of chyle (Schulman *et al.*, 1978). In our case, the presence of obstruction rather than laceration of the upper cisterna chyli was proved by the slow flow up the lateral para-aortic chains into the well distended cisterna chyli, the retrograde flow into its gastromesenteric tributaries, and the late appearance of free contrast medium in the peritoneal cavity. Obstruction was incomplete as shown by the appearance of some medium in the thoracic duct, which was sparsely opacified and showed no stasis or retrograde flow into tributaries (Schulman *et al.*, 1978). The cisterna chyli could only be described as well-distended but this fits in with our previous experience that, even in the presence of thoracic duct obstruction severe enough to produce retrograde flow with chylous effusions, the thoracic duct and cisterna chyli are not elastic enough to becomes dilated beyond normal limits (Schulman *et al.*, 1978).

REFERENCES

BIGLEY, H. A., Jr., and CHENAULT, O. W., Jr., 1975. Chylous ascites following retroperitoneal lymphadenectomy. *Journal of Urology*, *114*, 948–950.

BOYD, D. P. and WOOLDRIDGE, B. F., 1955. Chylous ascites, a postoperative complication. *Lahey Clinic Bulletin*, *9*, 105–107.

BRADHAM, R. R., GREGORIE, H. B. and WILSON, R., 1970. Chylous ascites following resection of an abdominal aortic aneurysm. *American Surgeon*, *36*, 238–240.

Clain, A., 1971. Chylous ascites following vagotomy. *British Journal of Surgery*, *58*, 312–314.

Cox, W. D., Schmitz, R. L. and Gillesby, W. J., 1966. Unusual complications of vagotomy and pyloroplasty—chylous ascites and achalasia (case reports). *American Journal of Surgery*, *32*, 259–260.

Freund, H., Brewster, D. and Fischer, J. E., 1979. Total parenteral nutrition in post-Warren shunt chylous ascites (letter). *Archives of Surgery*, *114*, 345.

Herz, J., Shapiro, S. R., Konrad, P. and Palmer, J., 1978. Chylous ascites following retroperitoneal lymphadenectomy. *Cancer*, *42*, 349–352.

Hocking, M. A. and Barth, C. E., 1978. Chylous ascites: a complication of vagotomy. *Journal of the Royal College of Surgeons of Edinburgh*, *23*, 232–233.

Ikard, R. W., 1972. Iatrogenic chylous ascites. *American Surgeon*, *38*, 436–438.

Klippel, A. P. and Hardy, D. A., 1971. Post-operative chylous ascites. *Missouri Medicine*, *68*, 253–255.

Maywood, B. T., Goldstein, L. and Busuttil, R. W., 1978. Chylous ascites after a Warren shunt. *American Journal of Surgery*, *135*, 700–702.

Miedema, E. B., Bissoda, N. K., Finkbeiner, A. E. and Casoli, R. E., 1978. Chylous ascites complicating retroperitoneal lymphadenectomy for testis tumors: management with peritoneovenous shunting. *Journal of Urology*, *120*, 377–378.

Musgrove, J. E., 1972. Postvagotomy abdominal chylous fistula. *American Surgeon*, *175*, 67–69.

Ross, G., Terry, B. E., Thompson, I. M., Beyer, P., 1971. Urologic aspects of chylous ascites. *Missouri Medicine*, *68*, 312–316.

Roy, J. B., Abdulian, M. and Walton, K. N., 1970. Chylous ascites. *Journal of Urology*, *103*, 343–344.

Schulman, A., Fataar, S., Dalrymple, R. and Tidbury, I., 1978. The lymphographic anatomy of chylothorax. *British Journal of Radiology*, *51*, 420–427.

Spence, C. R., Solomon, H. D., Agee, R. E. and Gangai, M. P., 1977. Chylous ascites—an unusual complication following retroperitoneal lymphadenectomy for testis tumor. *Journal of Urology*, *117*, 676–677.

Walker, W. M., 1967. Chylous ascites following pancreatoduodenectomy. *Archives of Surgery*, *95*, 640–642.

Warren, W. D., 1978. Ascites and portosystemic shunt. *American Journal of Surgery*, *135*, 607.

Warwick, R. and Williams, P. L., 1973. In *Gray's Anatomy*. (Longman, Edinburgh), 516–517, 1021–1022.

Books received

Receipt of the following books is acknowledged as a courtesy to the senders.

ABC Radiodiagnostic. 2. Radiologie des voies urinaires. By M. Barth and A. Dufour, pp. 104, 1979 (Masson, Paris).
ISBN 2-225-63690-7/ISSN 0181-0057

An Introduction to the Physics of Diagnostic Radiology (2nd Edit.) By E. E. Christensen, T. S. Curry and J. E. Dowdey, pp. xiii+428, 1978 (Henry Kimpton, London), £12·60.
ISBN 0-8121-0636-9

From "Quantity of Radiation" and "Dose" to "Exposure" and "Absorbed Dose"—An Historical Review. The Lauriston S. Taylor Lecture Series in Radiation Protection and Measurements. By Harold S. Wyckoff (NCRP), $7.00.
ISBN 0-913392-53-7

Advances in Space Research. Life Sciences and Space Research. Vol 1. pp. 232, 1981 (Pergamon, Oxford/New York), £12·50.
ISBN 0-0802-8396-9

Fundamentals in Technical Progress (International Symposium, Liège, May 1979). Vol. 1: Echographie/Ultrasound; Vol. 2: Dose planning; Vol. 3: Nuclear medicine; Vol. 4: Echographie/Ultrasound (French and English text) (Presses Universitaires de Liège).

Mutual Emergency Assistance for Radiation Accidents, IAEA, pp. 345, 1980.

The last four items have been placed in the Library of The British Institute of Radiology for the use of members.

1981, *British Journal of Radiology*, 54, 919–920 OCTOBER 1981

Short communications

Synergism of X irradiation and radiographic contrast medium

By *D. Carr, M.B., Ch.B., M.R.C.P.(UK), D.M.R.D., F.R.C.R., †A. Walker, B.Sc.(Hons.), ‡A. J. Tannahill, M.B., Ch.B. and §†R. G. White, D.M., F.R.C.P.(Glasg.), F.R.Path., F.R.S.E.

***X-ray Department, †University Department of Bacteriology and Immunology and ‡University Department of Pathology, Western Infirmary, Glasgow**

(*Received March 1981 and in revised form June 1981*)

Radiographic contrast media (RCM) are more toxic in animals with endotoxaemia (Slivka *et al.*, 1978). External abdominal X irradiation releases endotoxin from gut (Taketa, 1962). We have investigated the effect of large doses of abdominal X irradiation and intravenous meglumine ioglycamate in rabbits to determine whether or not the effects are additive.

Seven groups of white endotoxin-negative New Zealand rabbits (weight 2.1 to 2.9 kg) were studied (Groups A–G). The groups were treated with various combinations of external abdominal X irradiation and intravenous meglumine ioglycamate (Table I). The radiation was administered with a Dynaray 4, 4 MeV linear accelerator (Radiation Dynamics Ltd.), FSD 100 cm, field size 15 × 10 cm, dose measured at depth of 10 cm from skin surface. Meglumine ioglycamate was administered intravenously via an ear vein at a rate of 1 g/min. The experiments on Groups B and D were repeated, substituting ^{125}I-labelled meglumine ioglycamate for ordinary meglumine ioglycamate. All the animals in Groups B to G inclusive were examined macroscopically and histologically, either at death or after killing, three days after the procedure.

Histological sections were made of liver, kidney, spleen, adrenal, duodenum, small bowel, heart and lungs. The animals which had received ^{125}I-labelled meglumine ioglycamate were killed two hours after administration of RCM, and weighed samples of liver, kidney, spleen and plasma were placed in a scintillation counter and counted for five minutes. Endotoxin assays using the limulus technique (Levin and Bang, 1964) were performed on the plasma of all rabbits. Samples were taken before irradiation or injection of contrast medium and then at 0.5, 2 and 24 h after irradiation and/or injection of contrast.

RESULTS

There were no deaths in Groups A and B (Table I). One rabbit in Group C died five days after irradiation. The other 14 animals in Group C remained well. However, in Group D, nine animals out of 15 died (60%). Five died within 24 h of irradiation, two within 48 h and the other two within 72 h. In Group E there were no deaths. In Group F, seven rabbits out of ten died, six within 24 h and the other at 30 h. There were no deaths in Group G. There were no macroscopic or histological abnormalities in any of the animals in Groups B, C, E or G. In Group D there were no macroscopic abnormalities but eight of the animals showed signs of pulmonary oedema, three animals had necrotic foci in the white pulp of the spleen and two animals had necrotic foci in the peri-portal regions of the liver. In Group F there were no macroscopic abnormalities, but six of the animals showed signs of pulmonary oedema, two had necrotic foci in the white pulp of the spleen and two had necrotic foci in the peri-portal regions of the liver.

Table II shows that animals which had received abdominal X irradiation 2 h before RCM administration retained a significantly larger amount of RCM (^{125}I-labelled meglumine ioglycamate), in the kidney, liver, spleen and plasma compared to animals which had received RCM with no prior X irradiation. The differences between Groups A and B are

TABLE I

RESULTS OF RABBIT EXPERIMENTS

	A	B	C	D	E	F	G
Number in each group	15	15	15	15	10	10	10
Deaths	0	0	1	9	0	7	0
Histological abnormalities	None	None	None	Pulmonary oedema (8). Necrotic foci in spleen (3). Necrotic foci in liver (2).	None	Pulmonary oedema (6). Necrotic foci in spleen (2). Necrotic foci in liver (2).	None

A controls.
B 4.2 g/kg meglumine ioglycamate intravenously.
C 7.5 Gy (750 rad) abdominal X irradiation.
D 7.5 Gy (750 rad) abdominal X irradiation + 4.2 g/kg meglumine ioglycamate intravenously 2 h later.
E 4 Gy (400 rad) abdominal X irradiation.
F 4 Gy (400 rad) abdominal X irradiation + 4.2 g/kg meglumine ioglycamate intravenously 2 h later.
G 7.5 Gy (750 rad) abdominal X irradiation + 4.2 g/kg meglumine ioglycamate intravenously 24 h later.

---

§Present address: Department of Immunology, Addenbrooke's Hospital, Hills Road, Cambridge.

TABLE 2

Amount of iodine 125-labelled meglumine ioglycamate retained 2 hours post-injection (mean of five animals)

	Kidney	Liver	Spleen	Plasma
A	14500±1200	3600±400	18800±2000	12100±1500
B	22500±1200	8200±700	38800±2500	26000±2100
C	5000±550	2000±100	16800±1300	4200±200
D	6600±500	2300±150	8300±500	6000±4000

A 740 kBq (20 μCi) ^{125}I-labelled meglumine ioglycamate intravenously.
B 7.5 Gy (750 rad) of abdominal X-irradiation followed by 2 h later by 740 kBq (20 μCi) ^{125}I meglumine ioglycamate intravenously.
C 370 kBq (10 μCi) ^{125}I-labelled meglumine ioglycamate intravenously.
D 7.5 Gy (750 rad) of abdominal X irradiation followed 24 h later by 370 kBq (10 μCi) ^{125}I meglumine ioglycamate intravenously.
The numbers in the table are the counts in five min per g of material or per ml of plasma. Uncertainties are standard errors.

significant ($p < 0.01$, using Student's t-test). There is no significant difference between Groups C and D, *i.e.* RCM alone and RCM 24 h post-irradiation. The endotoxin assays were uniformly negative apart from one positive result in Group D and one positive result in Group F (both at 2 h post-RCM administration), but this is not statistically significant.

Comment

Abdominal X irradiation releases endotoxin from gut (Taketa, 1962) and the possibility that the deaths were due to endotoxic shock was considered. However, there was no evidence of endotoxic shock in any of the animals at post-mortem.

Endotoxin assays were generally negative, and it would therefore appear that endotoxin does not play a significant role in the mortalities recorded. Fumarola (1978) suggested that some RCM samples may be contaminated with endotoxin, but on testing several bottles of meglumine ioglycamate we found no positive results for endotoxin using the limulus assay. The pulmonary oedema may be due to a simple volume-overloading effect, *i.e.* the hyperosmolar RCM is not being excreted at the normal rate and attracts fluid into the intravascular compartment, leading to pulmonary oedema. The necrotic foci in the spleen and liver are not in the typical sites associated with septic emboli. These foci may be due to a pyaemic infection, the cause for which is not apparent. A significant point is that there were no deaths in Group G, *i.e.* RCM administered 24 h after X irradiation.

This suggests that the synergistic effect of RCM and X irradiation is transient, *i.e.*, the changes induced by the irradiation are short-lived, possibly representing a transient impairment of hepatic function. There was no pathological evidence of disseminated intravascular coagulation and pathological examination of the gut revealed no abnormality in any of the animals. We have confirmed that in human plasma, known reactors to RCM have a faster prekallikrein/kallikrein conversion rate than controls (E. Lasser, San Diego, personal communication), and it is possible that the RCM and X irradiation are additive in their release of kinins, and this may contribute to mortality. X irradiation alone has been shown to activate the clotting and kinin systems (Pouchova *et al.*, 1978) and RCM activates the clotting system (Lasser *et al.*, 1979), so it would seem reasonable that the additive effect we have demonstrated could be mediated via the clotting and kinin systems. The results suggest that large doses of abdominal X irradiation and biliary intravenous radiographic contrast medium act synergistically. The exact mechanism is uncertain, but is partially explained by the data from the radio-labelled RCM experiments showing that prior abdominal X irradiation delays excretion of the RCM, perhaps leading to toxic plasma and tissue levels. The necrotic splenic and hepatic foci may be secondary to impairment of the animals' resistance and reflect their overall poor condition. Stenstrand and Edgren (1981) have shown *in vitro* that low-dose X irradiation and RCM together cause an increase in chromosome aberrations, which suggests that the synergistic effect we have demonstrated could be a result of protein configurational changes. Further experiments are required to elucidate the time-course of the loss of interaction between RCM and X irradiation, and as there is no difference in mortality between 4 and 7.5 Gy (400 and 750 rad) it is important to discover the lowest radiation dose at which the synergy occurs.

It is difficult to extrapolate results to humans but it would seem prudent to exercise caution in the administration of biliary radiographic contrast medium to patients who are undergoing or have just undergone a course of radiotherapy.

Acknowledgments

This work was supported by a research grant from the Biomedical Research Committee of the Scottish Home and Health Department. The authors would like to thank Dr. A. C. McCartney for performing the endotoxin assays, and the staff of the Department of Clinical Physics and Bio-engineering, 11 West Graham Street, Glasgow. The authors wish to express thanks to Schering Chemicals Limited, Burgess Hill, West Sussex for their generous donation of the contrast media.

REFERENCES

Fumarola, D., 1978. Possible role of contaminating endotoxin in radiographic contrast media reactions (letter). *Investigative Radiology*, *13*, 554.

Lasser, E. C., Slivka, J., Lang, J. H., Kolb, W. P., Lyon, S. G., Hamblin, A. E. and Nazareno, G., 1979. Complement and coagulation: causative considerations in contrast catastrophies. *American Journal of Roentgenology*, *132*, 171–176.

Levin, J. and Bang, F., 1964. The role of endotoxin in the extracellular coagulation of limulus blood. *Bulletin of Johns Hopkins Hospital*, *115*, 265–274.

Pouckova, P., Pospisil, J. and Diestbier, Z., 1978. Changes of the kallikrein-kinin system in the course of the post-irradiation syndrome in rats and guinea pigs. *Czechoslovak Medicine*, *1*, 238–246

Slivka, J., Lasser, E. C., Lang, J. H., Lyon, S. G. and Hamblin, A. E., 1978. Effect of endotoxemia on contrast media reactions. *Investigative Radiology*, *13*, 21–25.

Stenstrand, K. and Edgren, J., 1981., Cytogenetic in vivo and in vitro effects of low dose radiation and contrast agents. *European Journal of Radiology*, *1*, 76–78.

Taketa, S. T., 1962. Water-electrolyte and antibiotic therapy against acute (3–5 days) intestinal radiation death in the rat. *Radiation Research*, *16*, 312–326.

1981, *British Journal of Radiology*, *54*, 921–922 OCTOBER 1981

OER and RBE variation between p(75)–Be and d(50)–Be neutron beams

By J. Van Dam, Ph.D.

Laboratorium voor Gynaecologische Cancerologie en Experimentele Radiotherapie en Dienst voor Gezwelziekten, K.U. Leuven, A.Z. St. Rafaël, B-3000 Leuven

and A. Wambersie, M.D., Ph.D.

Unité de Radiothérapie et de Neutronothérapie, U.C.L. 5469, Cliniques Universitaires St-Luc, B-1200 Bruxelles (Belgium)

(*Received April 1981 and in revised form May 1981*)

Neutron beams produced by 50 MeV deuterons on a 10 mm thick beryllium target have been used routinely for clinical applications at the cyclotron "CYCLONE" (Louvain-la-Neuve) since March 1978 (Wambersie *et al.*, 1979a). The depth-dose curves, as well as the surface build-up, are similar to those obtained with X rays of about 6 MV.

In order to improve further the physical selectivity of our irradiations, the use of neutron beams produced by bombarding a thick beryllium target with 75 MeV protons is contemplated. As an indication, the 50% dose is obtained at a depth of 16 cm for the present d(50)-Be neutrons and at a depth of 21 cm for the p(75)-Be neutrons with a 33 mm thick Be target and an additional 10 cm thick polyethylene filter (16 cm × 20 cm field, SSD = 158 cm).

However, prior to their clinical applications, and besides the necessary dosimetric measurements, the radiobiological characteristics of the p(75)-Be neutron beams have to be investigated. In this respect, the present paper compares the OER and the RBE of p(75)-Be and of d(50)-Be neutrons. On the one hand, it should be checked that increasing the neutron energy (and improving the physical selectivity of the irradiations) does not bring with it the drawback of an increase in OER. On the other hand it is necessary to evaluate the difference in RBE between the two beam qualities.

Growth inhibition in *Vicia faba* bean roots has been used as biological system in the present experiments. The different aspects of our technique have already been described (Van Dam *et al.*, 1980). This system is particularly suitable for OER determination; as regards RBEs, any observed differences should be regarded as upper limits of those expected for systems related to mammalian cell lethality (Hall and Rossi, 1975).

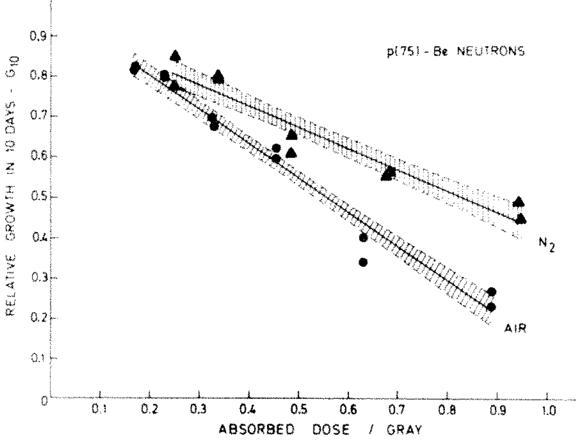


FIG. 1.

Relative growth in ten days (G_{10}) plotted as a function of absorbed dose after irradiation with p(75)-Be neutrons under aerobic and hypoxic conditions. Each point represents the mean of about ten roots. The slopes of the dose-effect relationships have been computed by regression analysis (see text); the hatched areas correspond to $\pm 2s_m$.

A total number of 600 roots (Sutton's Seeds) were irradiated after randomization with respect to radiation quality, oxygenation conditions and absorbed dose level. The reported absorbed doses are total absorbed doses $D_{n+\gamma}$ in Shonka type TE medium (Wambersie *et al.*, 1979b). The γ component was 7% in the d(50)-Be neutron beam, and preliminary measurements suggest that it was not very different in the p(75)-Be neutron beam. The dose rates were adjusted to be similar for both radiation qualities *i.e.* 0.1 Gy min^{-1}.

Our data are presented on Figs. 1 and 2 for p(75)-Be and d(50)-Be neutrons respectively. In the dose range investigated, the dose/effect relationships were found to be linear and straight lines were fitted through the experimental points by linear regression analysis.

The quoted OER values are the dose ratios corresponding to a relative growth G_{10} of 0.6. No significant difference was found between p(75)-Be and d(50)-Be neutron beams (Table I): OER = 1.5 (s_m = 0.1) and 1.4 (s_m = 0.1) respectively. In previous experiments (Van Dam *et al.*, 1980), an OER value of 1.5 (s_m = 0.1) was found for d(50)-Be neutrons and an OER value of 2.6 (s_m = 0.1) for ^{60}Co γ irradiation. The present results on *Vicia faba* are also in agreement with those obtained in the same beams at "CYCLONE" by Guichard *et al.* (1980) using V79 cells *in vitro;* they are also compatible with the data of Hall and Kellerer (1979) who

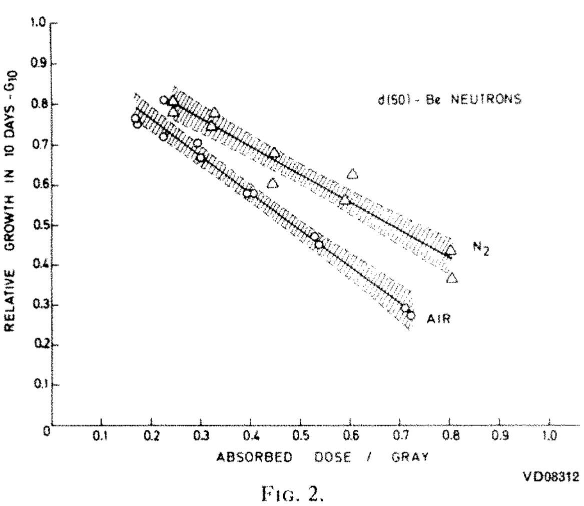


FIG. 2.

Same presentation as in Fig. 1 but for d(50)-Be neutrons.

TABLE I

OER AND RBE OF P(75)-BE AND D(50)-BE NEUTRON BEAMS

Radiation quality	OER ($\pm s_{\text{m}}$)*	Oxygen gain factor	References
I. OER studies			
p(75)-Be neutrons	1.5 ($\pm$0.1)	1.8†	Present results
d(50)-Be neutrons	1.4 ($\pm$0.1)	1.9†	Present results
d(50)-Be neutrons	1.5 ($\pm$0.1)	1.8	Van Dam *et al.*, 1980
Cobalt 60 γ rays	2.6 ($\pm$0.1)	—	Van Dam *et al.*, 1980

Radiation quality	Absorbed dose/Gy‡	RBE ($\pm s_{\text{m}}$)*	References
II. RBE/dose relationships			
p(75)-Be neutrons	0.25	0.85 ($\pm$0.15)	Present results
(relative to d(50)-Be neutrons)	0.4	0.85 ($\pm$0.1)	
	0.75	0.9 ($\pm$0.1)	
d(50)-Be neutrons	0.25	4.1 ($\pm$0.2)	Van Dam *et al.*, 1980
(relative to Cobalt 60 γ rays)	0.4	3.6 ($\pm$0.1)	
	0.75	3.0 ($\pm$0.2)	

Biological system: growth inhibition in *Vicia faba* (Sutton's Seeds). Cyclotron CYCLONE (Louvain-la-Neuve).

*s_{m} = standard error of the mean.

†With reference to the OER value for ^{60}Co γ rays quoted below.

‡Total absorbed dose $D_{\text{n}+\gamma}$ for the test radiation.

found only a slight increase in OER with incident particle energy in the present energy range.

The RBE of p(75)-Be neutrons with respect to d(50)-Be neutrons decreased from 0.9 ± 0.1 to 0.85 ± 0.15 for p(75)-Be neutron absorbed doses decreasing from 0.75 to 0.25 Gy. These results agree with those reported by Guichard *et al.* (1980) on V79 cells *in vitro* and by Wambersie *et al.* (1981) for chromosome aberrations in *Allium cepa* onion roots. For this latter system RBE decreased from 0.9 to 0.75 with decreasing p(75)-Be neutron doses from 0.5 to 0.04 Gy.

ACKNOWLEDGMENTS

The authors are pleased to thank Mrs. M. Octave-Prignot and Dr. J. P. Meulders who performed the dosimetric measurements. They would also like to thank Professor J. Bonte and Miss G. Billiet for their help and encouragement.

REFERENCES

GUICHARD, M., GUEULETTE, J., MEULDERS, J. P., WAMBERSIE, A. and MALAISE, E. P., 1980. Biological intercomparison of d(50)-Be and p(75)-Be neutrons. *British Journal of Radiology*, *53*, 991–995.

HALL, E. J. and ROSSI, H., 1975. The potential of Californium-252 in radiotherapy. *British Journal of Radiology*, *48*, 777–790.

HALL, E. J. and KELLERER, A., 1979. Review of RBE data for cells in culture. In *High LET Radiations in Clinical Radiotherapy*. Ed. by G. W. Barendsen, J. J. Broerse and K. Breur. *Supplement to European Journal of Cancer* (Pergamon Press, Oxford), pp. 171–174.

VAN DAM, J., BILLIET, G., WAMBERSIE, A., BRIDIER, A., DUTREIX, A. and BOUHNIK, C., 1980. RBE of d(50)-Be neutrons and of 650 MeV helium ions at different depths for growth reduction in *Vicia faba*. *Radiation Research*, *81*, 31–47.

WAMBERSIE, A., MEULDERS, J. P., RICHARD, F. and WINANT, M., 1979a. The fast neutron therapy facility at CYCLONE, Louvain-la-Neuve. In *High LET Radiations in Clinical Radiotherapy*. Ed. by G. W. Barendsen, J. J. Broerse and K. Breur. *Supplement to European Journal of Cancer* (Pergamon Press, Oxford), pp. 145–146.

WAMBERSIE, A., LAUBLIN, G., OCTAVE-PRIGNOT, M. and MEULDERS, J. P., 1979b. RBE of d(50)-Be neutrons for induction of chromosome aberrations in *Allium cepa* onion roots. *Strahlentherapie*, *155*, 776–785.

WAMBERSIE, A., LAUBLIN, G., MEULDERS, J. P., and OCTAVE-PRIGNOT, M., 1981. RBE variations between p(75)-Be and d(50)-Be neutrons determined for chromosome aberrations in *Allium cepa* (in preparation).

1981, *British Journal of Radiology*, 54, 923–924

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Radiosensitivity of lymphocytes separated from rat lymph nodes and human peripheral blood

THE EDITOR—SIR,

As a criterion for inactivation of lymphocytes after irradiation, loss of capacity for stimulation after addition of mitogens such as PHA is often used (Conrad, 1969; Carson *et al.*, 1965). A simple measure of stimulating ability is the incorporation of radioactive thymidine into DNA, measured by liquid scintillation counting after addition of PHA. This method has been found useful in estimation of whole-body absorbed dosage in man. For human lymphocytes isolated from peripheral blood, the radiosensitivity has been well established (Ilberty *et al.*, 1971; Baral and Blomgren, 1976; 1978). Similar measurements could be useful also with lymphocytes separated from animals. In particular, if more sensitive lymphocytes than those from human peripheral blood could be isolated, they might represent a more accurate *in vivo* dosemeter at low radiation doses.

In the present experiments a technique was established for the isolation of lymphocytes from rat lymph nodes. The radiosensitivity of these lymphocytes was investigated and compared with the radiosensitivity of lymphocytes separated from peripheral human blood.

Human lymphocytes were taken from heparinized venous blood of healthy persons (20 IU of heparin without preservation/ml blood). The lymphocytes were separated by differential centrifugation on a Ficoll-Hypaque gradient (Lymphoprep, Nyegaard & Co, Oslo) (Bøyum, 1968). After separation the cells were treated as described by Heier (1974). The human cells were grown in medium RPMI1640 without HEPES, supplemented with 15% AB serum.

Rat lymph nodes were taken from inbred Wistar Kyota rats anaesthetized with ether. The lymph nodes were collected in medium RPMI 1640 with HEPES supplemented with 5% rat serum. The serum was taken from the same type of inbred rats as the cells, though not from the same animals. With a hypodermic needle the membranes of the lymph nodes were ruptured and the lymphocytes suspended in the medium. To remove lymph node material the suspensions were filtered through 100 μm filter (Nytal, Schweizerische Seidengazefabrik AG). The cells were then washed three times in medium RPMI 1640 without HEPES and the cell number was counted in an electronic cell counter. Rat lymphocytes were grown on medium RPMI 1640 without HEPES, supplemented with 5% rat serum.

The cells were irradiated with 220 kV X rays at a dose rate of about 2 Gy/min. Unirradiated controls and irradiated samples were then diluted and plated in microwells (Falcon). Immediately afterwards PHA was added to give a final concentration in the wells of 16.6 μg/ml before the cells were incubated with CO_2. Once an hour up to 90 hours (methyl-^{3}H)thymidine was added to groups of three parallel wells to give a final activity in the well of 230 kBq (6.25 μCi)/ml. Thirty minutes after addition of (methyl-^{3}H)thymidine the cells in the three parallel wells were harvested by a Skatron Multiple Cell Culture Harvester, which lyses the cells with distilled water. The radioactivity was counted in a liquid scintillation counter and the radiation response was measured as the relative incorporated activity in irradiated and unirradiated populations.

Since the rate of incorporation of (methyl-^{3}H)thymidine was measured once every hour during incubation both for the irradiated and the unirradiated cells the variation in relative activity with time was closely observed. For human lymphocytes the time course of the rate of incorporation was similar to that already published by various workers. For rat lymphocytes, oscillations in the rate of incorporation were seen both for the irradiated and the unirradiated cells. Data from one typical experiment are shown in Fig. 1. In panel A the time course of the amount of incorporated thymidine is shown for an unirradiated population and a population irradiated with 1 Gy. The corresponding relative activities were calculated and are shown in panel B.

Although the reasons for the oscillations are not known, we will suggest two possible explanations: (a) the oscillations might express a synchrony in the cycling population of stimulated cells. This is possible since it is known that PHA-stimulated lymphocytes are able to complete several cell cycles (Bender and Prescott, 1962; Marshall and Roberts, 1965; Jaksic *et al.*, 1976) and that the formation of cell suspensions from lymphoid tissue can induce selective loss of cells in a specific part of the cell cycle (Fossum *et al.*, 1979); (b) different subpopulations of lymphocytes could be stimulated at different times, giving rise to separate maxima in the overall DNA synthesis rate of the population.

Data similar to those shown in Fig. 1B were recorded for both types of lymphocytes after various radiation doses. Mean values of the relative activity recorded during the period 50–75 hours after addition of PHA for the human cells and 40–70 hours after addition of PHA for the rat cells were calculated. These values are the experimental points of

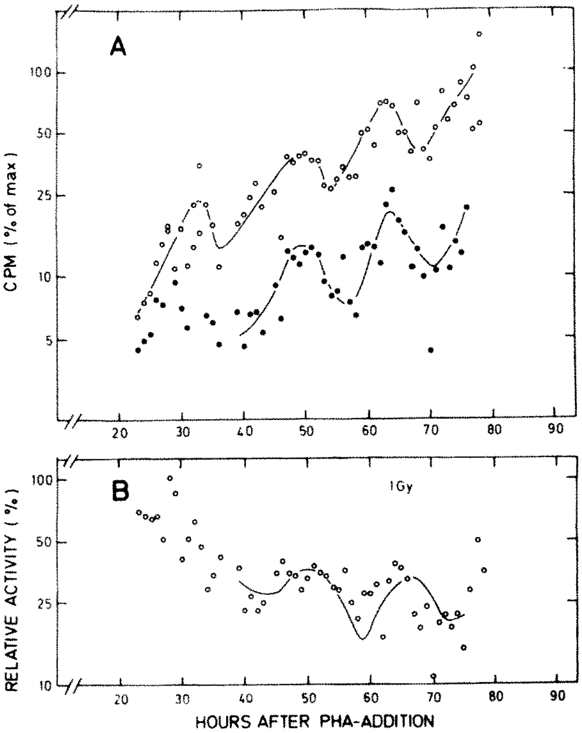


FIG. 1.

(A) Rate of DNA-synthesis of lymphocyte populations separated from rat lymph nodes as a function of the time after addition of 16.6 μg/ml of PHA. Data are shown for cells irradiated with 1 Gy (●) as well as for unirradiated cells (○). Both curves were drawn by hand.

(B) The relative rate of DNA-synthesis of the irradiated (1 Gy) and the unirradiated population as a function of time after addition of 16.6 μg/ml PHA.

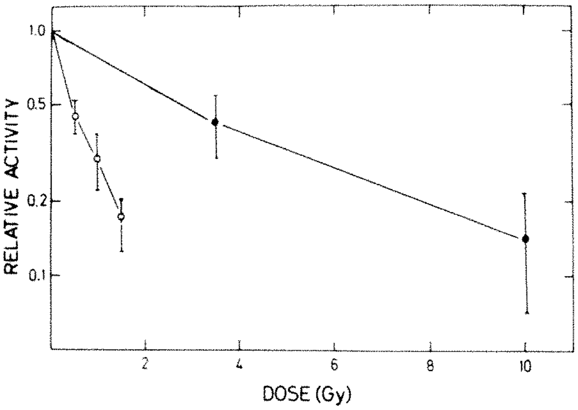


FIG. 2.

Dose-response curves of lymphocytes separated from human peripheral blood (●) and from rat lymph nodes (○). The experimental points represent the mean of all observations of relative activity during the time intervals 50–75 h and 40–70 h after addition of PHA for the human and rat cells respectively. The error bars represent standard deviations.

the dose-response curves shown in Fig. 2. The error bars represent standard deviations.

The data indicate that the human lymphocytes from peripheral blood are clearly more resistant than the rat lymphocytes from lymph nodes. For a comparative response, the human cells need about six times the radiation dose required by the rat cells. Thus, as a biological dosemeter, the cells from the rat lymph nodes offer a higher sensitivity than the cells from peripheral human blood. Due to the oscillations in the rate of incorporation of ^{3}H-thymidine, however, the need for standardization during measurements is even higher with the rat cells.

Yours, etc.,

*E. O. PETTERSEN,
†K. J. OLSEN,
†A. B. JACOBSEN,
‡A. B. ANDERSEN.

Departments of *Tissue Culture and ‡Haematology,
Norsk Hydro's Institute for Cancer Research,
and the †General Department,
The Norwegian Radium Hospital,
Montebello, Oslo 3, Norway.

(*Received March 1980 and in revised form June 1981*)

REFERENCES

BARAL, E. and BLOMGREN, H., 1976. Response of human lymphocytes to mitogenic stimuli after irradiation *in vitro. Acta Radiologica Therapy Physics and Biology, 15,* 149–161.

1978. Time factor in PHA responsiveness of human blood lymphocytes after *in vitro* irradiation. *Acta Radiologica Therapy Physics and Biology, 17,* 138–144.

BENDER, M. A. and PRESCOTT, D. M., 1962. DNA synthesis and mitosis in cultures of human peripheral leucocytes. *Experimental Cell Research, 27,* 221–229.

BØYUM, A., 1968. Separation of leucocytes from blood and bone marrow. *Scandinavian Journal of Clinical and Laboratory Investigation, 21,* Supplement 97, 1–108.

CARSON, G. A., SARKANY, I., WILLIAMS, H. S., TODD, A. P. and GRELL, H. M. C., 1965. Radioactive method for the measurement of lymphocyte transformation *in vitro. Lancet, i,* 1266–1268.

CONRAD, R. A., 1969. Quantitative study of radiation effects in phytohaemagglutinine-stimulated leucocyte cultures. *International Journal of Radiation Biology, 16,* 157–165.

FOSSUM, S., ROLSTAD, B. and TJERNSHAUGEN, H., 1979. Selective loss of S-phase cells when making cell suspensions from lymphoid tissue. *Cellular Immunology, 48,* 149–154.

HEIER, H. E., 1974. The influence of mechanical force on the rosette test for human T lymphocytes. *Scandinavian Journal of Immunology, 3,* 677–681.

ILBERY, P. L. T., RICKINSON, A. B. and THRUM, C. E., 1971. Blood lymphocyte replicating ability as a measurement of radiation dosage. *British Journal of Radiology, 44,* 834–840.

JAKSIC, B., PAGLIARDI, G. L. and PEGORARO, L., 1976. Kinetics of phytohaemagglutinine stimulated lymphocytes in chronic lymphocytic leucemia. *Cell Tissue Kinetics, 9,* 419–428.

MARSHALL, W. H. and ROBERTS, K. B., 1965. Continuous cinematography of human lymphocytes cultured with a phytohaemagglutinin including observations on cell division and interphase. *Quarterly Journal of Experimental Physiology, 50,* 361–374.

Book review

Renal Adenocarcinoma. A series of workshops on the biology of human cancer. Report No. 10, pp. 215, 1980 (UICC Technical Report Series. Vol. 49) (International Union Against Cancer, Geneva), Sw.fr. 17.
ISBN 92-9018-049-8

This is an interesting and useful collection of papers covering clinical and research aspects of renal adenocarcinoma. It is a moderately uncommon tumour comprising less than 2% of all cancers, so that a small publication indicating the present position is to be welcomed. Known factors which play a role in the aetiology, together with other possible agents, are considered and all the text is well supported by references to the literature.

There is a section on the radiological approaches to the diagnosis and treatment of the tumour, which is a concise summary of the present position of diagnostic radiology in this context. It is not a book with radiological illustrations but it is easy to read and should stimulate one to look elsewhere for more detailed information. There is a particularly good account of the latest views on the histopathology of this carcinoma.

On the research side, coverage is given to spontaneous hormonal and chemically induced animal models of this tumour as well as information about viral models and the latest views about immune mechanisms and steroid receptors.

The paperback concludes with a chapter on the chemotherapy of renal adenocarcinoma and thoughts for future studies.

B. T. HALE.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 36 Portland Place, London W1N 3DG.

Fellowships and Grants for Cancer Research

The International Union against Cancer invites applications for Yamagiwa-Yoshida Memorial International Cancer Study grants (deadline December 31) and International Cancer Research Technology Transfer Programme Grants. Details and application forms from: UICC, rue du Conseil-General 3, 1205 Geneva, Switzerland.

The International Agency for Research on Cancer (World Health Organization) invites applications for training fellowships in 1982/3 from junior scientists wishing to be trained in the fields of epidemiology, biostatistics and environmental carcinogenesis (both chemical and viral). Details and application forms from: The Head of the Research Training and Liaison Programme, 150 cours Albert-Thomas, 69372 Lyon Cedex 02, France. Deadline January 31 1982.

The Short and Long Term Biological Consequences of Exposure to Radiation

Middlesex Hospital, London. Tuesday, October 13, 1981. Enquiries to the Programme Committee Secretary, Professor J. H. Martin, Department of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

A Changing Role for Radiotherapy in the Treatment of Small Cell Carcinoma of the Bronchus

At the BIR, 36 Portland Place, London W1N 3DG, on Thursday, October 15 at 7.15 p.m. Chairman: Professor R. J. Berry; speakers: Professor N. M. Bleehan, Mr. J. Belcher and Dr. I. E. Smith. Preceded (5.45 p.m.) by a State of the Art Seminar on "Lung cancer: the clinical problem" (Chairman: Mr. W. M. Ross).

Radiobiology Work-in-Progress Meetings

Meetings during the coming year at the Institute include "Subcellular targets, including ultrastructural damage", November 20, 1981; a general meeting on February 26, 1982 and "Late damage to normal tissues after radiotherapeutic doses" on May 21, 1982. The all-day Saturday meeting will be on November 21, 1981, on "The effects of small doses—the basis of radiation protection".

Please note all meetings will be held at the BIR's new address, 36 Portland Place, London W1.

The Radiological Diagnosis and Treatment of Thyroid Disease

Wednesday, November 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held at the Institute, 36 Portland Place, London W.1. The meeting will cover all aspects of thyroid disease, including the use of isotopes.

Interventional Arteriographic Procedures

At the BIR, 36 Portland Place, London W1N 3DG, on Thursday, November 19 at 7.15 p.m. Speakers: Drs. D. J. Allison, M. Collins and D. Cumberland. Preceded (5.45 p.m.) by a State of the Art Seminar on "ECRP: the radiologist's approach" (Chairman: Dr. M. I. Lavelle).

Safety Review and Inspection of Nuclear Power Plants

The International Atomic Energy Agency will hold a seminar in Vienna from November 23–27, 1981. Further information and participation forms from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4OJ (phone 01–211 6850).

Paediatric Radiology 1981

Great Ormond Street, London, November 26–27

This annual two-day course is designed for consultants and senior registrars. The theme will be the gut; other topics covered will include jaundice, hypertension and the neonatal big head. Speakers will include paediatricians, paediatric surgeons and endoscopists; there will be opportunity for open discussion.

There are a limited number of places. Cost £40. Full details: Dr. I. Gordon, Department of Paediatric Radiology, Hospital for Sick Children, Great Ormond Street, London WC1 (telephone 01–405 9200). Closing date for applications November 10.

Combined Modality Therapy—Clinical and Laboratory Aspects

A joint meeting (British Institute of Radiology and British Association for Cancer Research) will be held on November 26 and 27 at The Royal College of Surgeons, Lincoln's Inn Fields, London. Speakers: Professor N. M. Bleehan, Drs. R. Sandland, L. L. Gunderson, W. H. Shipley, J. Overgaard, S. Dische and Professor P. Alexander (the 2nd Gordon Hamilton-Fairley Memorial Lecture). Enquiries to: Dr. M. J. Embleton, Cancer Research Campaign Laboratories, University of Nottingham, University Park, Nottingham NG7 2RD.

4th Annual Mid-Winter Meeting

American Endocurietherapy Society

December 9–11, 1981

The Fourth Annual Mid-Winter Meeting of the American Endocurietherapy Society will commence at the Wailea Beach Hotel, Maui, Hawaii, on December 9, 1981. The scientific programme features symposia, workshops and scientific sessions dealing with the many aspects of cancer management utilizing interstitial and/or intracavitary radiation therapy for sites such as the breast, head and neck, uterine cervix, prostate, among others. Guest speakers include Professor Daniel Chassagne from the Institut Gustave-Roussy, Villejuif, France; Eric Hall, D.Phil., College of Physicians and Surgeons, Columbia University, New York; and Professor Yasushi Shigematsu, Department of Radiology, Osaka University, Osaka, Japan.

Scientific sessions on specific disease sites will be conducted every morning. Abstracts for proffered papers should be mailed to the Executive Offices of the American Endocurietherapy Society no later than October 15. This meeting has been approved for 15 hours Category 1 CME credit by the California Medical Association. For further information, write to: American Endocurietherapy Society, 1245 Wilshire Blvd., Suite 217, Los Angeles, California, 90017. Attn: Norma Kaysing, Executive Secretary.

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1.

Forthcoming events and notices

Radiation Biology for Part I F.R.C.R. Radiotherapy and Oncology

An intensive course in radiation biology will be held in the Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester, January 25–29, 1982, inclusive. The course follows the syllabus for the Part I F.R.C.R. examinations. Although the course is intended primarily for radiotherapists in training it is also open to students of radiation biology and experimental oncology. Lectures and demonstrations will be given by the staff of the Paterson Laboratories. Applications: Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX.

Quantities and Units for use in Radiation Protection

Scientific meeting and exhibition, National Physical Laboratory, Teddington, Middlesex, Tuesday, January 26, 1982. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

The Mayneord Symposium

Friday, February 19, 1982. This meeting is being organized by, the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. It will be an all-day meeting to be held at the Royal Society, in Carlton House Terrace, London. The theme for the meeting will be "The future in radiology" as seen by distinguished workers in a number of branches of radiological science.

The Natural Radiation Environment

Tuesday, March 30, 1982, at the Central Electricity Generating Board, Sudbury House, 15 Newgate Street, London EC1. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

European Society of Pediatric Radiology
19th Congress, Prague, April 22–24, 1982

Organized by the European Society of Pediatric Radiology, Czechoslovak Medical Society J. E. Purkyně, Czechoslovak Radiologic Society and the Czechoslovak Pediatric Society. Deadline for applications and abstracts: December 30, 1981. Information: Czechoslovak Medical Society J. E. Purkyně, 19th Congress of the European Society of Pediatric Radiology, Vítězného února 31, 120 26 Praha 2, Czechoslovakia.

The Association of Radiologists of West Africa

Will hold its 20th Annual Conference in Benin City, Nigeria, May 5–8, 1982. Full information from: Dr. J. C. Odita, Department of Radiology, University of Benin Teaching Hospital, P.M.B. 111, Benin City, Nigeria, West Africa.

Society for Radiological Protection
Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01-486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on The contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A. M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

5th South African International Radiological Congress

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas participants, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

7th International Congress of Radiation Research

Will be held at the International Congress Centre RAI, Amsterdam, The Netherlands, July 3–8, 1983. Information: Dr. J. J. Broerse (Secretary-general of the 7th ICRR), Radiobiological Institute TNO, PO Box 5815, 2280 HV Rijswijk, The Netherlands.

Book reviews

A practical introduction to cranial CT 849

Manuel de techniques radiographiques du crâne 849

Nuclear medicine—focus on clinical diagnosis 855

Scintillation camera acceptance testing and performance evaluation 855

Basic bone radiology 860

Lumbale Myelographie mit wasserlöslichen Kontrastmitteln 874

Lecture notes on clinical oncology 881

Roentgenology of lymphomas and leukemias 881

The effects on populations of exposure to low levels of ionizing radiation 898

Cancer 898

Diagnostic radiation: a possible factor in malignancy in patients with cronic inflammatory bowel disease 904

Cancer risks by site 904

Choix d'un systéme informatique pour le calcul des doses en radiotherapie 908

Renal adenocarcinoma 924

Books received 918

RADIATION PROTECTION of the PATIENT

A Manual of Good Practice

Edited by : Walter A. Langmead

Part I. — Diagnostic Radiology

Price £2.95

This Manual is concerned with the radiation protection of patients undergoing diagnostic examinations or treatment with ionising radiations. It examines the responsibilities of the many individuals – general practitioners, clinicians, radiologists, radiographers and physicists – whose special fields of knowledge together contribute to the radiation safety of the patient, and it proffers advice to each in turn as to the preferred procedures to minimise the patient's radiation dose without reducing the level of diagnostic achievement or the efficacy of treatment.

The Manual is to be published in two Parts, dealing with radiology and with nuclear medicine and radiotherapy. PART I. – DIAGNOSTIC RADIOLOGY, covers the X-ray examination from the initial request to the final report. The scientific and technical factors which enable the clinical objectives to be attained with minimal dose to the patient are also reviewed. Two Appendices give recommendations respectively for certain specialised X-ray examinations, and for a departmental guide to radiographic procedures.

The benefits of medical diagnosis and treatment with radiation are large and the potential radiation hazards arising therefrom are comparatively minor in most cases. Nevertheless, the safety of the patient is paramount and this results from good teamwork and attention to detail, as outlined in this Manual.

Prepared by Panels of the British Radiological Protection Association; and published by The British Institute of Radiology.

Orders to BIR Publications, 36 Portland Place, London W1N 3DG.

VOL 54 NO 646 OCTOBER 1981

The British Journal of Radiology

Contents

Page

The noes have it! Do they? Silvanus Thompson Memorial Lecture 1981. 831
J. Mallard

Rapid biomedical imaging by NMR. 850
R. J. Ordidge, P. Mansfield and R. E. Coupland

The investigation of chest disease in children by high kilovoltage filtered beam radiography. 856
J. E. Deanfield and A. R. Chrispin

Radiology and risk: an economist's perspective. 861
G. H. Mooney

Ultrasound features of tumour thrombus in the IVC in retroperitoneal tumours. 866
S. J. Pussell and D. O. Cosgrove

An appraisal of the use of diagnostic ultrasound to quantify the lumbar spinal canal. 870
D. Finlay, H. R. Stockdale and E. Lewin

Monte Carlo calculation of the dose distributions across a plane bone-marrow interface during diagnostic X-ray examinations. 875
R. N. Kulkarni

Total-body irradiation in advanced non-Hodgkin's lymphoma. 878
H. J. Dobbs, A. Barrett, A. Y. Rostom and M. J. Peckham

European protocol for neutron dosimetry for external beam therapy. 882
J. J. Broerse, B. J. Mijnheer and J. R. Williams

Dose-effect relations for tumour control and complication rate after fast neutron therapy for pelvic tumours. 899
J. J. Battermann, G. A. M. Hart and K. Breur

Technical notes. 905
  Measurement of the lumbar spinal canal by diagnostic ultrasound.
    Catherine S. Hibbert, Carole Delaygue, Beatrice McGlen and R. W. Porter
  A technique for the loading of iridium 192 wire.
    L. R. Bridge, D. S. C. Marshall and W. P. Wilson

Case reports. 909
  The localization of bleeding small bowel lesions for conservative resection: a simple radiographic technique.
    J. M. Stevens, J. M. A. Northover, M. J. Raphael and W. W. Slack
  Therapeutic adrenal venous infarction in ACTH-dependent Cushing's syndrome.
    J. Rosenstock, D. Allison, G. F. Joplin, P. D. Lewis, K. Mashiter, R. B. Welbourn and M. C. White
  Lymphography in post-vagotomy chylous ascites.
    A. Schulman, I. N. Marks, D. M. Dent and A. H. Girdwood

Short communications. 919
  Synergism of X irradiation and radiographic contrast medium.
    D. Carr, A. Walker, A. J. Tannahill and R. G. White
  OER and RBE variations between p(75)–Be and d(50)–Be neutron beams.
    J. Van Dam and A. Wambersie

Correspondence. 923
  Radiosensitivity of lymphocytes separated from rat lymph nodes and human peripheral blood.
    E. O. Pettersen, K. J. Olsen, A. B. Jacobsen and A. B. Andersen

Forthcoming events and notices. 925

(*continued on inside back cover*)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
36 Portland Place, London W1N 3DG

ISSN 0007-1285
17143

14.982

Volume 54 Number 647
November 1981

THE BRITISH JOURNAL OF RADIOLOGY

X-ray diagnosis
Radiation oncology
Nuclear medicine
Ultrasound
Radiological physics
Radiobiology
Radiation protection
and related [illegible]

Published by
The British Institute of Radiology

The British Journal of Radiology

FOUNDED 1896

The Editorial Committee consists of:

The Editors:

J. L. HAYBITTLE, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
C. H. JONES, BSC., PH.D., F.INST.P.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., CH.B., F.R.C.R., F.R.A.C.R. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

ADVERTISEMENTS: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

SUBSCRIPTIONS: All communications should be sent to The British Institute of Radiology, 36 Portland Place, London W1N 3DG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

ANNUAL SUBSCRIPTION: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14). (From January 1, 1982: £65·00 ($145), single copies £7·00 ($16); postage extra on all orders received after April 30, 1982.)

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
PATRON: HER MAJESTY THE QUEEN

Founded 1897
36 PORTLAND PLACE, LONDON W1N 3DG
Telephone: 01–580 4085 and 580 4189. Cable Address: "Britology, London W.1."

President: M. J. DAY, B.A., PH.D.

Hon. Secretaries:

M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
JANET HUSBAND, M.R.C.P., F.R.C.R.

Hon. Treasurer: D. PACE

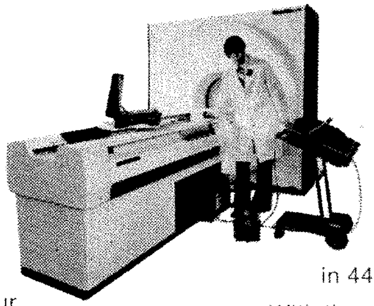
General Secretary: MRS. J. ROYSTON

THE BRITISH INSTITUTE OF RADIOLOGY is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981

Which company has the largest CT service force in Europe?

General Electric Company of U.S.A:*
Proven support for proven systems.



General Electric of U.S.A. Medical Systems is the leader — not only in Europe but throughout the world — in computed tomography (CT) technology. And, matching this capability is our in-depth service force... helping to maintain optimum clinical performance.

Specifically, more than 350 engineers, technicians and support personnel service our full line of imaging systems from operations in 12 European countries. Each specialist is factory trained at the GE Medical Systems Institute and provided refresher courses to keep current with new products and technologies. Franchised distributors maintain service organisations in six additional countries. Parts are stocked in 44 depots throughout Europe.

With thousands of diagnostic imaging systems — CT, x-ray, nuclear and ultrasound — already operating across Europe, General Electric U.S.A. is committed to providing the service needed to keep them performing efficiently.

Service that protects your equipment investment. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

Frankfurt/M., Tel.: 06 11/7 60 73 69 ● Wien, Tel.: 24 14 51 ● Brussel, Tel.: 660 2010 ● Kopenhagen, Tel.: 2 86 86 00 ● Mailand, Tel.: 753 1351 ●
Breda, Tel.: 76 22 54 15 ● Lissabon, Tel. 36 71 55 ● Madrid, Tel.: 252 5100 ●Goteborg, Tel.: 42 09 70 ● Zürich, Tel.: 47 50 30

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

RADIOLOGY TEACHING PROGRAMS

A series of programs designed for teaching radiology to medical undergraduates

The programs may be used as demonstrations, tutorials or library sources.

Clinical Programs
1. pulmonary consolidation
2. pulmonary collapse
3. pleural disease
4. mediastinal abnormalities
5. solitary lung nodules
6. multiple lung nodules
7. diffuse lung disease
8. intestinal obstruction

Anatomy Programs
1. thorax
2. skull
3. spine
4. upper extremity
5. lower extremity

Each program is composed of a number of 10"×12" transparencies which can be duplicated on standard radiographic copiers.

Cost: clinical programs – £15 including postage
anatomy programs – £20 including postage

Enquiries: Head of Department of Radiology,
University of Queensland, Clinical Sciences Building,
Royal Brisbane Hospital, Herston, Qld 4029,
Australia.

Diagnostic Ultrasound Course for Sonologists and Sonographers

An intensive two-week programme to emphasize the basic fundamentals of Diagnostic Ultrasound will be offered at the Health Science Centre, 700 William Avenue, Winnipeg, Manitoba, R3E 0Z3, by Dr. E. A. Lyons, Associate Professor of Radiology.
The programme provides lectures, evening scan sessions, daily scan sessions with patients and daily reading sessions of routine clinical material. The programme also offers access to a large teaching file, video-tape library and slide file. The lecturers are invited speakers and members of the permanent staff.

Dates:
September 14–25, 1981
November 23–December 4, 1981
January 25–February 5, 1982
April 12–23, 1982
June 7–18, 1982

Permanent Faculty:
Dr. E. A. Lyons, Associate Professor of Radiology
Dr. R. E. Brown, Associate Professor of Radiology
Dr. F. Manning, Associate Professor of Obstetrics and Gynecology

The programme meets the criteria for ACR category I credit for 68 hours per programme. Enrollment is limited to 15 participants per programme.

For further information please contact:

**Ms. Maureen Kostesky, Programme Co-ordinator,
Section of Diagnostic Ultrasound, 700 William
Avenue, Winnipeg, Manitoba, R3E 0Z3, Canada
Telephone: 1–204–787–3701**

OXFORD MEDICAL PUBLICATIONS

Oxford Medical Publications

Cunningham's Textbook of Anatomy

Edited by G. J. Romanes

In the new edition of this standard textbook of anatomy, the whole text has been reviewed and revised with regard to new developments in the study and teaching of anatomy. In addition, the sections on the central nervous system, digestive system, and respiratory system have been almost entirely rewritten. A completely new feature is the addition of an atlas of anatomical structure using radiograph and tomograph (CT scans) in addition to normal illustrations. Twelfth edition illustrated £25

A New System of Anatomy

being a Dissector's Guide and Atlas

Lord Zuckerman, with Deryk Darlington and Peter Lisowski

For this new edition of a standard dissection guide for medical students the revisers have simplified some of the dissections in line with modern anatomy curricula. They have rearranged the order of several dissections, notably the upper part of the neck, and rewritten and simplified the heart dissection. A new section on the brain has been added to deal with the practical problems of shortage of materials. Second edition illustrated £30
paperback £18·50

Oxford University Press

New: for the treatmen of malignant effusions

Coparvax is a freeze-dried preparation of Corynebacterium parvum. When injected into previously-aspirated pleural or peritoneal effusions, Coparvax has been shown to be extremely effective at preventing recurrence and easing the associated symptoms.

In addition, Coparvax has a remarkably low incidence of side-effects, unlike many other treatments, some of which may require concomitant narcotic analgesia.

For further information on this advance in the management of malignant effusions please contact our Scientific Services Division at the address below.

PRESCRIBING INFORMATION

Presentation Vial containing 7mg (dry weight of the inactivated *Corynebacterium parvum* organisms WFL strain CN 6134) with thiomersal, in a freeze-dried form. **Uses** Alleviation of malignant pleural effusions and malignant ascites. **Dosage** 7-14mg recommended, although some patients have responded to lower doses. **Administration** Freeze-dried Coparvax should be reconstituted with 1ml of physiological saline for injection and diluted in a further volume of 10-20ml prior to injection. The suspension should be injected, within 24 hours of reconstitution, into the pleural or peritoneal cavity via the paracentesis needle immediately after the effusion has been aspirated. Injection may be repeated, if necessary, at intervals of one to four weeks. **Contra-indications** During pregnancy, and patients with known hypersensitivity to thiomersal. **Precautions** The incidence and severity of side-effects attributable to Coparvax administered intrapleurally, appears to be intensified if given within 10 days of thoracotomy and lung resection probably due to enhanced systemic absorption of Coparvax. Coparvax should not be given during the immediate post-operative period. Following intrapleural or intra-abdominal administration, leakage of Coparvax into subcutaneous tissues may result in local tenderness. Intense fibrinous reaction in the pleural and peritoneal cavities has been observed following local administration of Coparvax. Intestinal obstruction due to the formation of adhesions is a theoretical possibility, although it has not been reported as a complication of Coparvax administration. **Adverse effects** Fever occurs in 10 to 40% of patients following intracavitary injection. Abdominal pain or mild abdominal discomfort has been reported in some 20% of patients following intraperitoneal instillation Nausea and vomiting may occur in a minority of patients following intracavitary administration of Coparvax. **Basic NHS Cost** Single vial (7mg), £30 (PL3/0097).

Coparvax*

Corynebacterium parvum

when the quality of life is the primary concern

Calmic Medical Division
The Wellcome Foundation Ltd.
Crewe, Cheshire
(Tel: 0270 583151)

*Trade Mark

ONTARIO CANCER FOUNDATION
TORONTO-BAYVIEW CLINIC
Sunnybrook Medical Centre

MEDICAL PHYSICISTS

The Toronto-Bayview Clinic is a new cancer treatment centre associated with Sunnybrook Hospital and the University of Toronto. Construction of the outpatient and radiation therapy facilities will be completed by October 1981.

The Clinic will treat 2500 new patients a year and will have a major research orientation. Radiotherapy equipment will include a Cobalt unit, one 6 MeV and two 25 MeV linear accelerators, simulator, and treatment planning computer. Support facilities will include a machine shop, electronics shop, and laboratory space for clinical physics and research.

There are three positions immediately open for Clinical Physicists with appropriate training or experience in medical physics and radiation therapy treatment planning. Applications are encouraged from Ph.D., M.Sc. and B.Sc. medical physicists with suitable qualifications. In addition to clinical responsibilities, physicists may be involved in teaching and in research.

Interested individuals are encouraged to respond promptly, and to send a curriculum vitae and the names of three referees to: Dr. H. B. Michaels, Head, Division of Clinical Physics, Ontario Cancer Foundation, Toronto-Bayview Clinic, 2075 Bayview Avenue, Toronto, Ontario M4N 3M5, Canada.

British Journal of Radiology Supplements

No.12 Carcinogenesis and Radiation Risk, a Biomathematical Reconnaissance

By W. V. Mayneord and R. H. Clarke

Reprinted 1979 **£6.50**

No.15 Computerized Tomographic Scanners in Radiotherapy in Europe

Edited by Roger J. Berry

1981 **£19.50**

No.16 Treatment Simulators (Applications of Modern Technology in Radiotherapy)

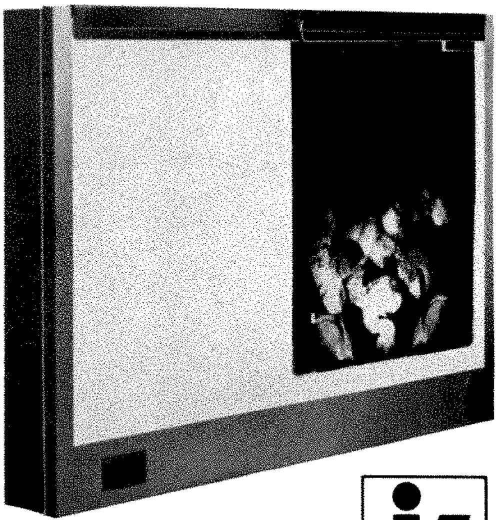
Revised 1981 **£3.50**

Available from:

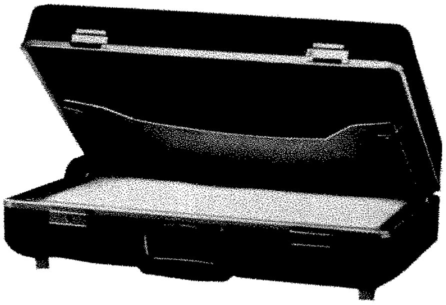
Publications Department,
British Institute of Radiology,
36 Portland Place,
London W1N 3DG **(01–580 4085)**

Please send remittance with order

See X-Rays in a new light.



J.K. LIGHTING have developed a special range of X-ray viewing light box's, together with an executive light case. Both of special interest to both doctors + dentists alike. Send this coupon now for our leaflet and price list."

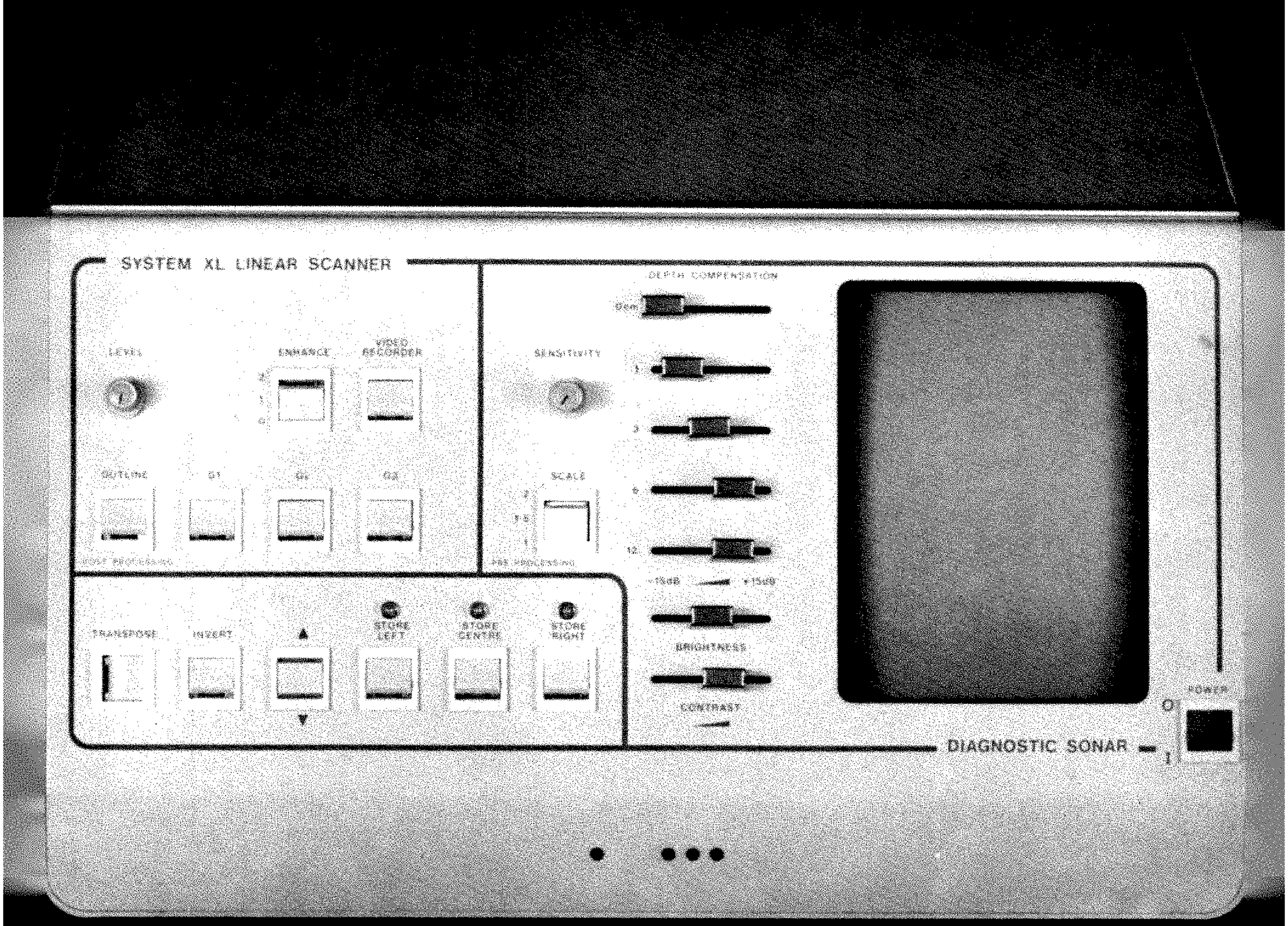


Tudor Works, Beaconsfield Road,
Hayes, Middlesex. Tel: 01-848 3661/2

JK
JENRICK

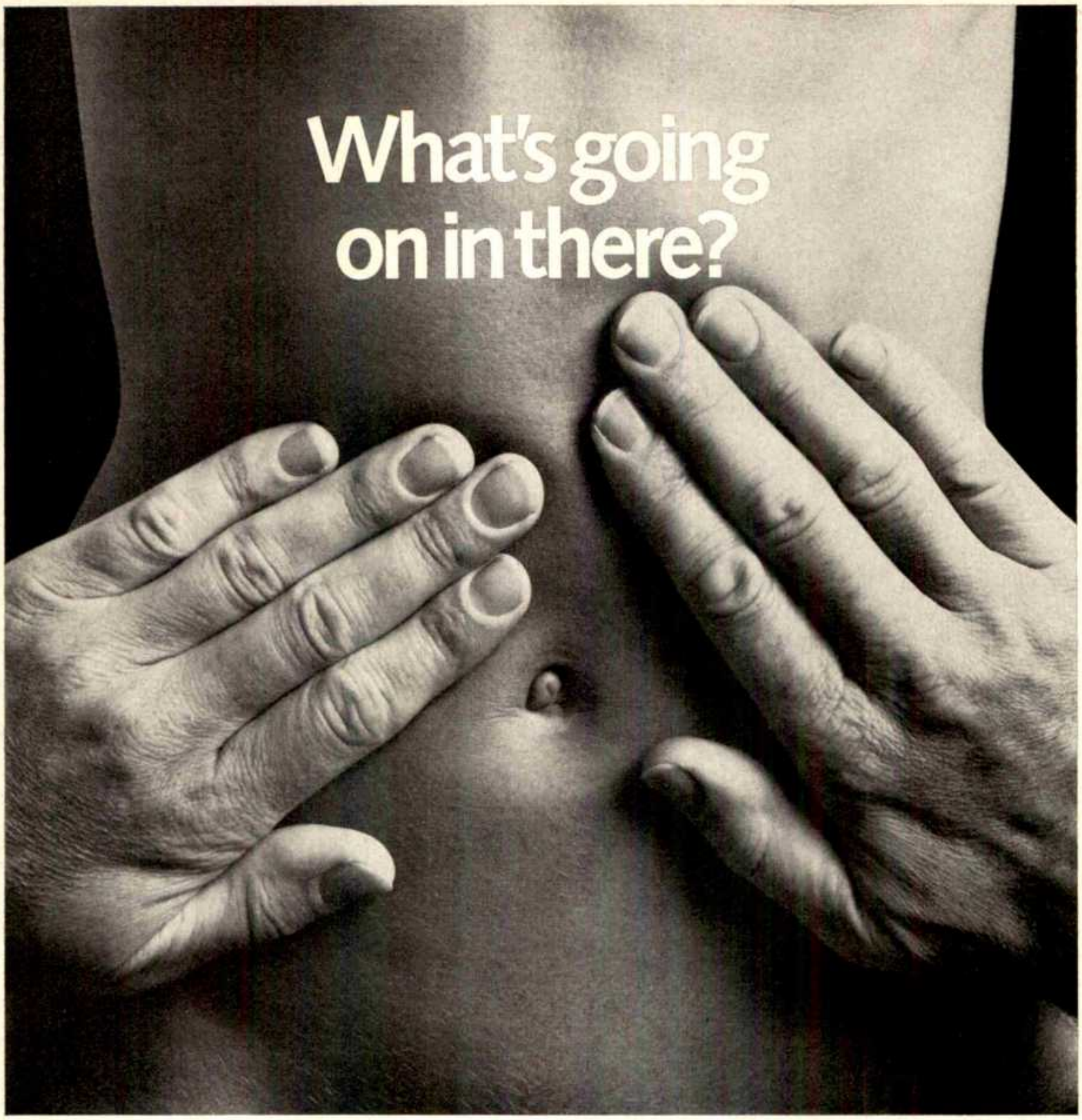
Please send me your full colour brochure. J K Lighting Displays Ltd.
Tudor Works, Beaconsfield Road, Hayes, Middlesex. Tel: 01-848 3661/2
Name ....
Address ....
J. K. Lighting Displays Ltd.

SYSTEM XL



ULTRASONIC EXCELLENCE
IN REAL TIME LINEAR SCANNERS

DIAGNOSTIC SONAR
Baird Road, Kirkton Campus, Livingston EH54 7BX, Scotland
Telephone: 0506 411877. Cables: Sonar Livingston. Telex: 72591 DSONAR G.


What's going on in there?

Trust baritop to tell you

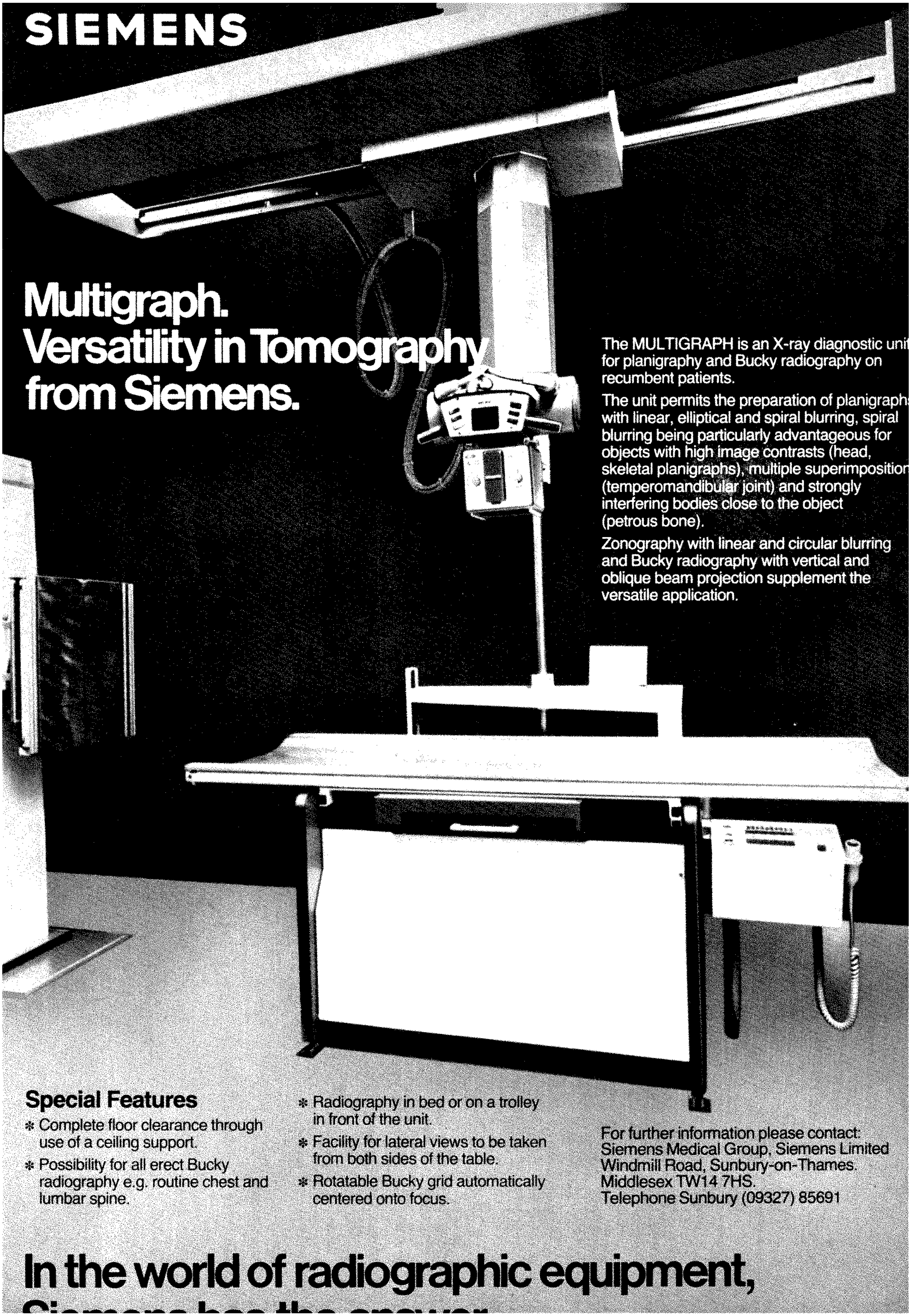
Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.

SIEMENS



Multigraph.
Versatility in Tomography
from Siemens.

The MULTIGRAPH is an X-ray diagnostic uni for planigraphy and Bucky radiography on recumbent patients.

The unit permits the preparation of planigraph with linear, elliptical and spiral blurring, spiral blurring being particularly advantageous for objects with high image contrasts (head, skeletal planigraphs), multiple superimpositio (temperomandibular joint) and strongly interfering bodies close to the object (petrous bone).

Zonography with linear and circular blurring and Bucky radiography with vertical and oblique beam projection supplement the versatile application.

Special Features

- ✻ Complete floor clearance through use of a ceiling support.
- ✻ Possibility for all erect Bucky radiography e.g. routine chest and lumbar spine.
- ✻ Radiography in bed or on a trolley in front of the unit.
- ✻ Facility for lateral views to be taken from both sides of the table.
- ✻ Rotatable Bucky grid automatically centered onto focus.

For further information please contact:
Siemens Medical Group, Siemens Limited
Windmill Road, Sunbury-on-Thames.
Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691

In the world of radiographic equipment,
Siemens has the answer

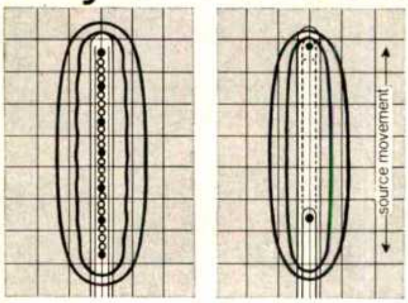
An afterloading system for intracavitary and interstitial radiotherapy using Ir 192 or Cs 137.

Afterloading Buchler

Isodose distributions can be obtained by using one single oscillating source or by using fixed source-trains or series of selected sources and inactive beads.

Buchler makes use of the first method* to be able to offer you effectiveness, a lower investment price, an easier service and maintenance program and a quicker and safer source-exchange.

You always work with only one oscillating source



left:
source train or series of sources and inactive beads

right:
oscillating source

An additional aspect: with Afterloading Buchler you can change over from low dose to high dose at any time without altering the device – simply by changing the source.

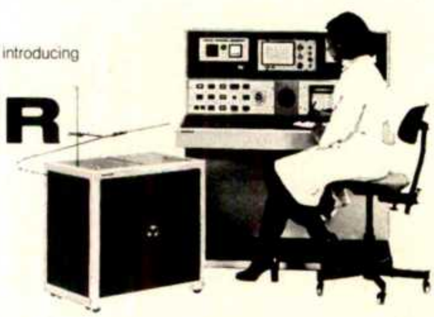
With Afterloading Buchler you decide on an oscillating source giving you many advantages.

*) For the 3-channel device with two additional stationary sources.

Please let us know if you want to know more about introducing or changing to the »Buchler« Afterloading method.

BUCHLER

Buchler GmbH
Bereich Radioaktivität und Strahlenschutz
D-3300 Braunschweig   Harxbütteler Straße 3
Telefon (0 53 07) 18 65   Telex 09 52 533



Automatic, Computer-controlled Dynamic and High Resolution Static B-scanning

The Sonography System RA-1 diagnostic ultra-sound scanner uses sophisticated, computer-controlled image processing to achieve superior image resolution. The advanced, state-of-the-art scanheads comprise:

⁕ LFOV scanheads for multiformat abdominal scanning.
⁕ WV scanheads for high frame-rate scanning.
⁕ Small parts scanhead, incorporating Doppler with Spectral Analysis, for superficial vessel and organ studies, for neonatal and paediatric scanning.

The modular design guards against obsolescence whilst permitting expansion and the ability to retrofit new imaging techniques as they are developed.

Universal Computer-controlled High Resolution Static B-scanning

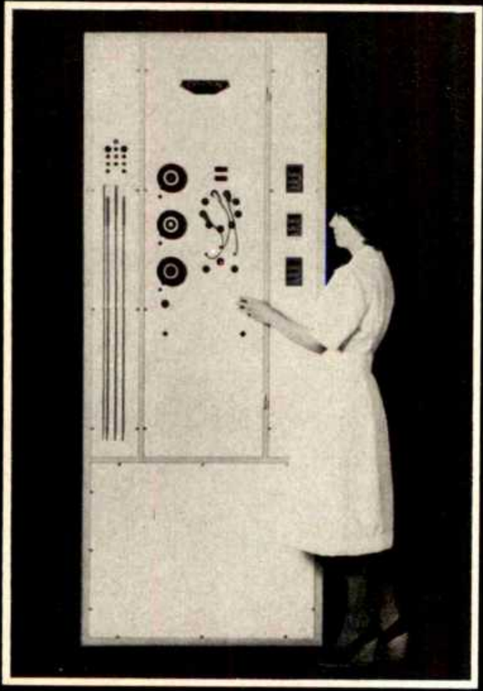
The Universal Pho/sonic-SM fully-integrated computer-controlled, high performance ultrasound scanner which produces excellent image resolution. It is designed to meet individual requirements through a variety of system options, including:

⁕ Wide range of transducers ⁕ Image Process Functions
⁕ Area, Circumference and Volume measurements.
⁕ Obstetrics measurement facility ⁕ Floppy disc interface

Future improvements to the image processing may be incorporated due tc the flexible computer software.

Other Siemens ultrasound equipment is available, including the IMAGER 2300, a Dynamically Focused Linear Array Real-Time B-scanner.
For full details write to: Siemens Medical Group, Siemens Limited, Windmill Road, Sunbury-on-Thames, Middlesex TW14 7HS.
Telephone Sunbury (09327) 85691.

...Siemens gives you the choice!

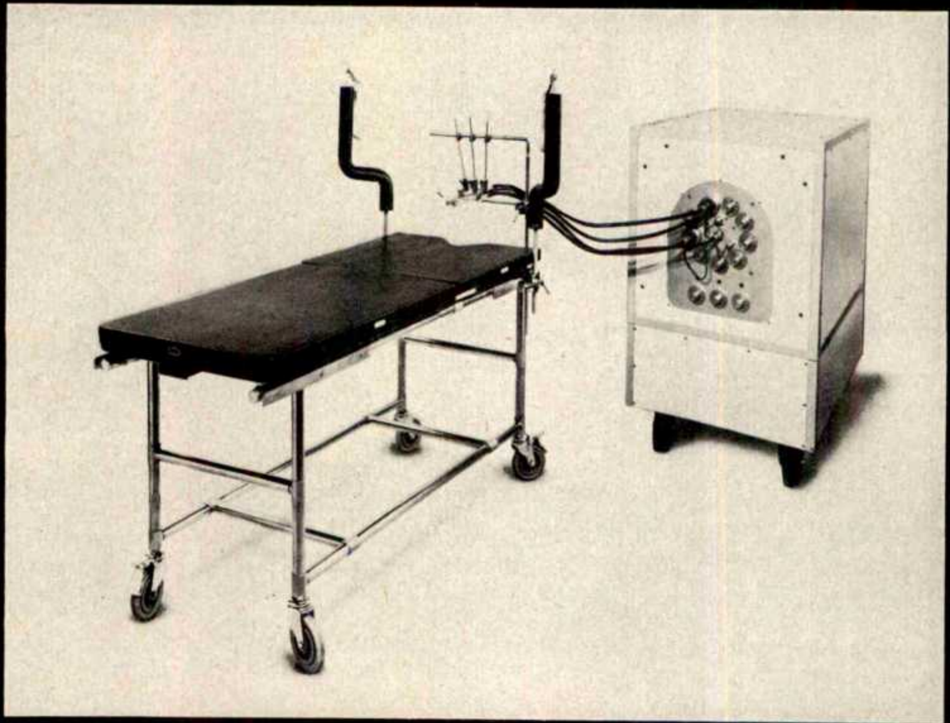


Cathetron
Remote loading Intracavitary unit using Cobalt 60.

The Cathetron has now been in clinical use for over a decade and is used by well over 30 hospitals in nearly 20 different countries.

Use of the Cathetron gives full protection, from radiation hazards, to all staff and reduces treatment time to minutes, thus ensuring that the Catheters stay in their correct location. These short treatment times mean that many patients can be treated as out-patients and therefore need not take up valuable bed space.

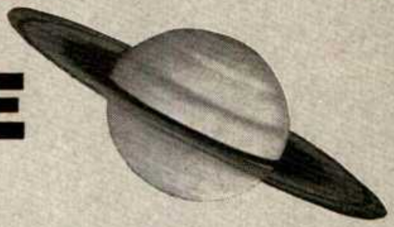
The Cathetron is used for surface mould treatments; treatments of the oesophagus and bronchi as well as gynaecological cases.

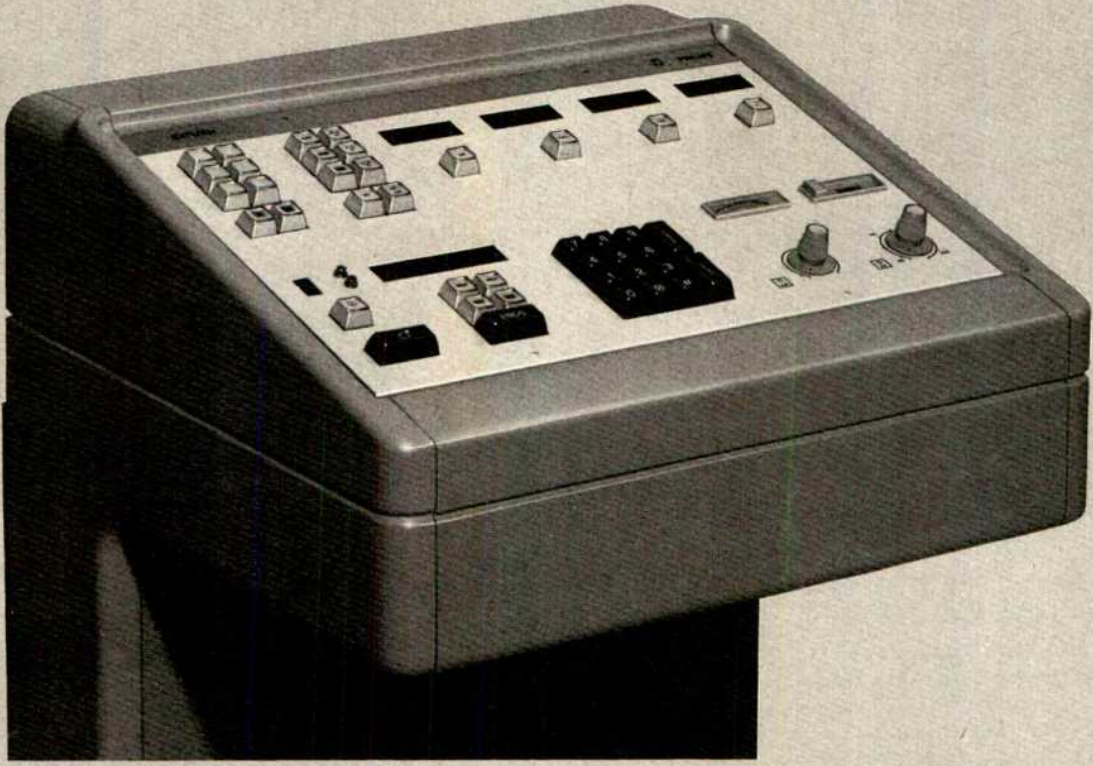


TEM Instruments Limited

Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex 87397, Grams TESTMENT CRAWLEY

THE COMPUTERIZED GENERATOR OF TOMORROW IS HERE TODAY





SATURN–

THE MICROPROCESSOR CONTROLLED GENERATOR

FLEXIBILITY
- One, two or three factor control
- Operator input to memory store
- Over 200 operator introduced programmes
- Last exposure on each auxiliary memorised for instant recall

DIGITALLY DISPLAYED
- kV mA mAs time
- Post exposure of mAs and time
- Organ and projection
- Number of further exposures possible
- Diagnosed error or malfunction

PHILIPS

PHILIPS

Medical Systems

International course in gastro-intestinal radiology

Lund, Sweden June 14–18, 1982

Organizing committee: Erik Boijsen and Anders Lunderquist.

This postgraduate course will focus on the most up-to-date techniques in gastro-intestinal radiology including the gastro-intestinal tract, the liver, the bile ducts, the spleen and the pancreas. Diagnostic as well as interventional procedures will be covered. Morning sessions with formal lectures will be followed in the afternoon by workshops giving more time for informal discussions.

For further information, please contact:

Anders Lunderquist, M.D.
Department of Diagnostic Radiology
University Hospital
S-221 85 LUND
Sweden

Management of Malignant Disease Series

3 The Management of Testicular Tumours

Edited by Michael Peckham

This book deals with the biology, pathology and especially the treatment of testicular tumours. Dramatic improvements in treatment results are illustrated, the toxicity of treatment stressed and the desirability of defining groups of patients where non-aggressive treatment methods are effective, is discussed.
£17·50 boards 296 pages 89 illustrations
Publication 26 November

Also available in the series:

1 The Management of Terminal Disease
Edited by Dame Cicely M. Saunders
£11 boards 222 pages 26 illustrations

2 Malignancies of the Ovary, Uterus and Cervix
Raymond S. Bush
£13·95 boards 256 pages 77 illustrations

Edward Arnold
41 Bedford Square, London WC1B 3DQ

Diagnostic Radiologist

Diagnostic Radiologist wanted, with fellowship or eligible, to join radiological group in Edmonton, Alberta, Canada. Hospital and office practice. Applicant should have training in special procedures and/or ultrasound.

Please reply to:
Dr. W. J. Taylor, M.B., Ch.B., D.M.R., F.R.C.P.(C.)
#360 10830-Jasper Avenue
Edmonton, Alberta
Canada T5J 2B3

Fellowship in Brachytherapy

Two positions available July 1, 1982, with research and O.R. opportunities, emphasizing lung and prostate. Three years of radiotherapy training and VQE required.

Apply: Dr. Beryl McCormick,
Memorial Sloan-Kettering Cancer Center,
NYC, NY 10021.

CANADA

The Grenfell Regional Health Services are responsible for staffing an area, approximately the size of the British Isles, involving most of Labrador and Northern Newfoundland. It has a mixed population of 40,000 served by four hospitals and one of these is a teaching hospital affiliated to the Memorial University, Newfoundland. There are also medical centres and nursing stations.

Travel expenses from UK to Newfoundland are paid.

Applications are invited for

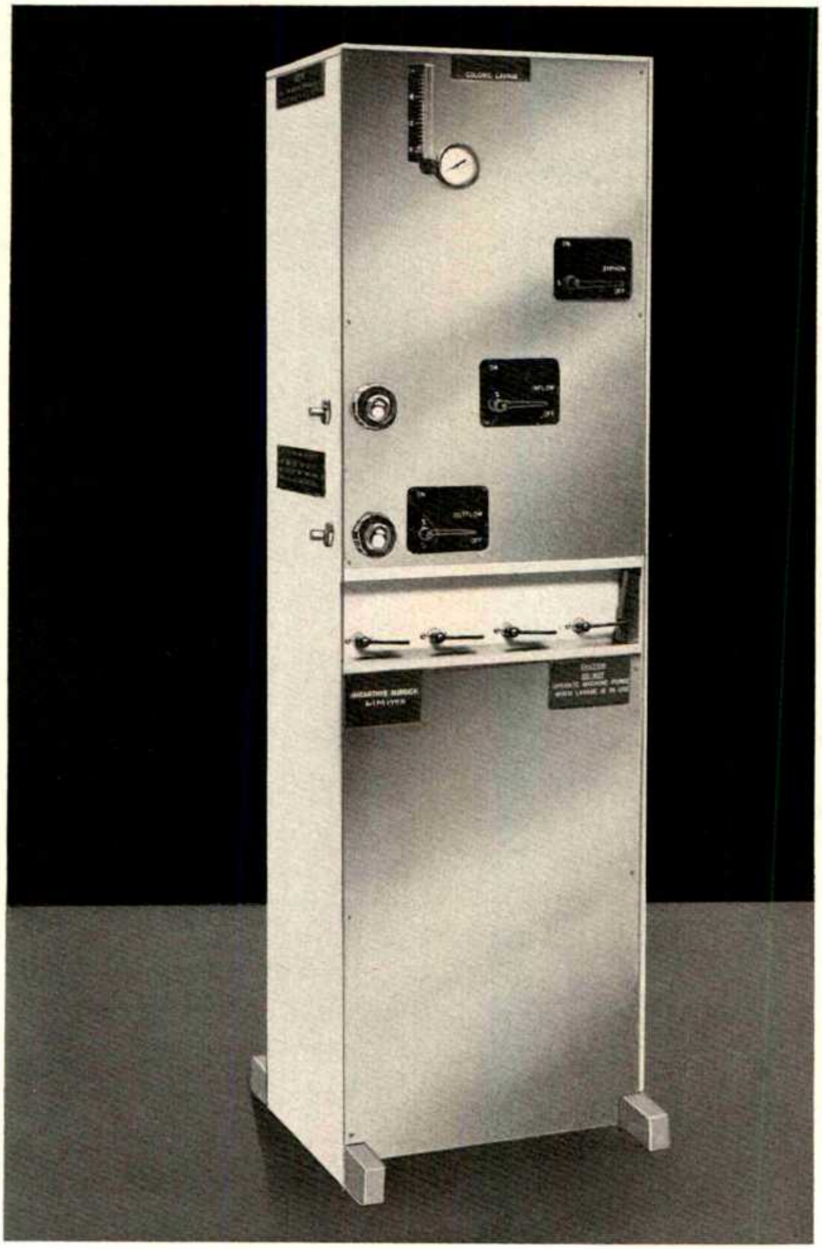
LOCUM RADIOLOGIST

This appointment will be of Consultant grade but a Senior Registrar with appropriate experience might be considered. The post is for one year from July 1982 at a salary of approximately $45,000 p.a. (Canadian dollars). The exact salary will depend on training and experience. The Radiologist will be based at the Charles Curtis Memorial Hospital, St. Anthony, where the population is 6,000.

UK applicants **only** are invited to apply to:
Grenfell (UK) Office, c/o Prof. Ivan Curson, KCH Dental School, Denmark Hill, London SE5 8RX

Applicants resident outside the UK should apply directly to:
The Personnel Director, Grenfell Regional Health Services, Charles Curtis Memorial Hospital, St. Anthony, Newfoundland A0K 4S0, Canada.

HENDERSON
COLONIC LAVAGE UNIT



The Henderson Colonic Lavage provides a simple, effective and safe apparatus for washing out the large intestine and the terminal ileum of the small bowel.

The Henderson Colonic Lavage is indicated for patient preparation prior to surgery or radiography.

An important feature of this machine is, that as fluid is withdrawn from the patient, air is admitted to maintain the full lumen of the bowel, permitting complete fluid evacuation and assisting further faecal removal.

Macarthys Surgical Ltd

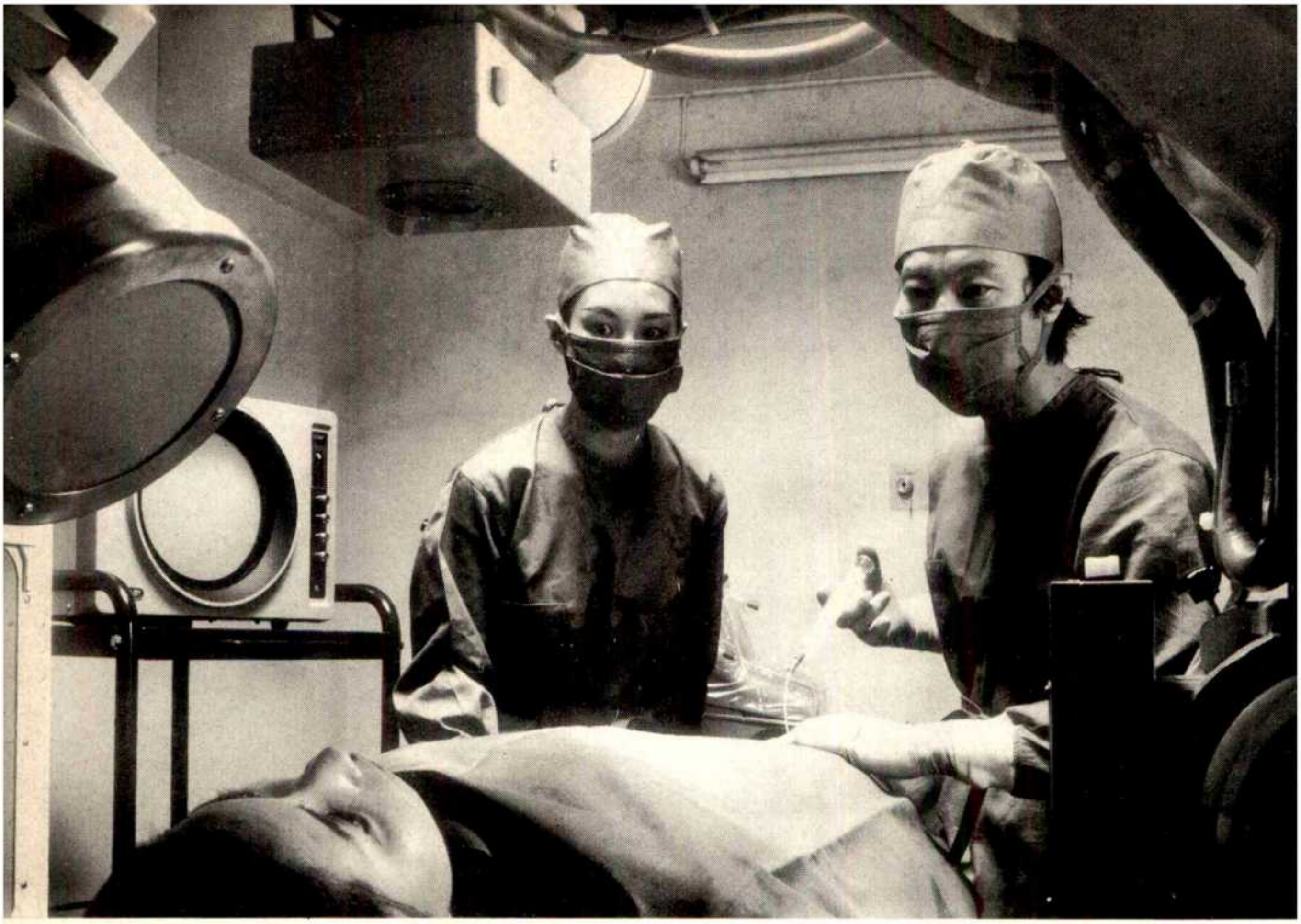
DAGENHAM
Selinas Lane
Dagenham, Essex RM8 1QD
Tel.: 01-593 7511

BIRMINGHAM
Unit 25/28
Edgebaston Shopping Centre
Hagley Road
Birmingham B16 8SH
Tel.: 021-454 6713

GLASGOW
301-3 Glentanar Road
Balmore Industrial Estate
Glasgow G22 7UG
Tel.: 041-336-8782

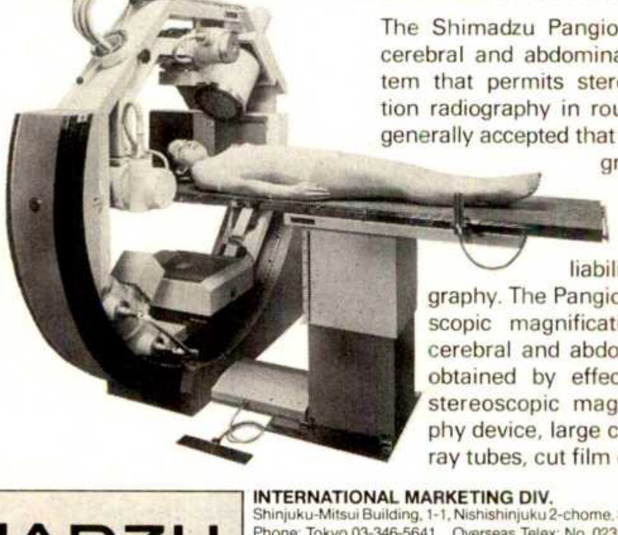
LIVERPOOL
201-3 London Road
Liverpool L3 8JS
Tel.: 051-207-1348

MANCHESTER
Precinct Centre
Oxford Road
Manchester M13 9GS
Tel.: 061-273-6754/5



PANGIOMAX

CEREBRAL AND ABDOMINAL ANGIOGRAPHY SYSTEM



The Shimadzu Pangiomax is a dedicated cerebral and abdominal angiographic system that permits stereoscopic magnification radiography in routine diagnosis. It is generally accepted that magnification radiography and stereography effectively increase the diagnostic reliability of cerebral angiography. The Pangiomax permits stereoscopic magnification images of the cerebral and abdominal vessels to be obtained by effectively combining a stereoscopic magnification radiography device, large capacity fine-focus x-ray tubes, cut film changers, etc.

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D.
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

New Volume in the Clinics in Diagnostic Ultrasound Series

Ultrasound in Emergency Medicine
Edited by Kenneth J.W. Taylor and
Gregory N. Viscomi
Volume 7 1981 218 pages
271 half-tone + 17 line illustrations hardback
£12.95

Deals fully and exclusively with the applications of diagnostic ultrasound to acutely ill patients. Featuring the contributions of 21 outstanding authorities in the field, the book covers a complete spectrum of emergency situations including those in ophthalmic, neurologic, cardiac, obstetrical, gynaecological and abdominal areas.

Volumes Already Available in the Clinics in Diagnostic Ultrasound Series

Diagnostic Ultrasound in Gastrointestinal Disease
Edited by Kenneth J.W. Taylor
Volume 1 1979 188 pages
153 half-tone illustrations hardback £12.95

Genitourinary Ultrasonography
Edited by Arthur T. Rosenfield
Volume 2 1979 264 pages
295 half-tone illustrations hardback £12.95

Diagnostic Ultrasound in Obstetrics
Edited by John C. Hobbins
Volume 3 1979 202 pages
99 half-tone illustrations hardback £12.95

Two-Dimensional Echocardiography
Edited by Joseph A. Kisslo
Volume 4 1981 222 pages
113 half-tone + 48 line illustrations
hardback £11.00

New Techniques and Instrumentation in Ultrasonography
Edited by P.N.T. Wells and Marvin C. Ziskin
Volume 5 1981 254 pages
98 half-tone + 80 line illustrations
hardback £12.00

Ultrasound in Cancer
Edited by Barry B. Goldberg
Volume 6 1981 234 pages
208 half-tone + 48 line illustrations
hardback £12.95

Churchill
Livingstone

Robert Stevenson House, 1-3 Baxter's Place,
Leith Walk, Edinburgh EH1 3AF

Forthcoming Volumes in the Series include:

Volume 8 **Diagnostic Ultrasound in Pediatrics**
edited by J.O. Haller and A. Shkolnik

Volume 9 **Case Studies in Ultrasound**
edited by Harris J. Finberg

Volume 10 **Real-time Ultrasonography**
edited by F. Winsberg and P. Cooperberg

Other Important Books

A Textbook of Radiology and Imaging
Edited by David Sutton
1980 Third edition Single Volume edition 1,456 pages hardback £65.00
Two Volume edition Volume I 698 pages Volume II 800 pages hardback £80.00
2,937 half-tone + 234 line illustrations

Neuroradiology
Edmund H. Burrows and Norman E. Leeds
1981 Two Volumes 944 pages
2,845 half-tone + 76 line illustrations
hardback £95.00

A major new text on the radiology of the brain and spinal cord, providing an informed approach to the radiological investigation and interpretation of neurological disorders.

Pearls in Diagnostic Radiology
Harold D. Rosenbaum
1981 252 pages 242 half-tone illustrations
hardback £19.50

Using a case-orientated approach, this book challenges the reader to reach a correct diagnosis on the basis of given radiological data.

Gynecologic Oncology
Fundamental Principles and Clinical Practice
Edited by Malcolm Coppleson
1981 Two-Volume Set 1,140 pages
62 full-colour + 552 half-tone + 51 line and tone + 259 line illustrations hardback £75.00

This definitive new work on malignant disease of the female genital tract provides encyclopedic treatment of the entire field

Scheduled for December Publication!

Scientific Basis for Medical Imaging
Edited by Peter N.T. Wells
1981 320 pages approx. 100 half-tone + 169 line illustrations hardback £25.00 approx.

Recent Advances in Clinical Oncology–1
Edited by C.J. Williams and J.M.A. Whitehouse
1981 352 pages approx 46 half-tone + 52 line illustrations paperback £19.50 approx.

Research & development

GUERBET

Better contrast media through research

Laboratoire GUERBET
16-24, rue Jean Chaptal - 93601 Aulnay-sous-Bois - Cedex FRANCE
Tél.: 866.78.37 - Télex: 212382 F.

1981, *British Journal of Radiology*, *54*, 927–931
VOLUME 54 NUMBER 647 NOVEMBER 1981

The British Journal of Radiology

Ultrasonography in acute cholecystitis

By F. Croce, M.D., G. Montali, M.D., L. Solbiati, M.D. and G. Marinoni, M.D.

Servizio di Radiologia, Ospedale di Circolo di Busto Arsizio, Via A. da Brescia, 21052 – Busto Arsizio (VA), Italy

(*Received April 1981*)

ABSTRACT

Forty cases of acute cholecystitis, surgically and pathologically confirmed, were investigated with ultrasound.

Echographic diagnosis was possible in 34 patients (85%): special emphasis was laid on wall thickening (90% of cases, with a mean wall thickness of 8.08 mm), evidence of an echofree layer within the wall (67.5% of patients) and a lumen greater than 4 cm with thick walls.

Associated cholelithiasis was demonstrated in 28 of these patients. In five more patients specific wall signs were absent and cholelithiasis was the only detectable sign of the disease. In only one patient was there no echographic sign of acute cholecystitis.

In the past few years grey-scale ultrasonography has been widely used for visualization of the gall bladder and detection of cholecystitis. More recently assessment of gall-bladder wall features has been considered an essential part of cholecystosonography, especially in acute and chronic cholecystitis (Engel *et al.*, 1980; Finberg and Birnholz, 1979; Handler, 1979; Marchal *et al.*, 1978). However, the usefulness of single echographic signs is still controversial (Fiske *et al.*, 1980; Sanders, 1980) or not fully defined (Engel *et al.*, 1980; Finberg and Birnholz, 1979).

This report describes our observations in 40 cases of acute cholecystitis, in an attempt to help delineate the echographic pattern of this disease.

PATIENTS AND METHODS

The study group consists of 40 patients, referred to our Ultrasound Department with a clinical suspicion of acute cholecystitis. Most patients had epigastric or right upper quadrant pain, tenderness and fever. Occasionally a painful mass could be palpated. All patients were investigated early after onset of symptoms and cholecystectomy was performed within 24 hours: acute cholecystitis was confirmed surgically and pathologically.

All ultrasound examinations were performed by a physician in longitudinal, transverse and oblique planes. A real time scanner (Aloka SSD 240) with a 3.0 MHz probe and a static scanner (PhoSonic SM Digital) with either a 3.5 or a 5.0 MHz transducer were used.

In the echographic evaluation of acute cholecystitis we considered four main features.

1. Thickening of the gall-bladder wall, defined as measuring 3 mm or greater (Engel *et al.*, 1980; Finberg and Birnholz, 1979; Handler, 1979). Wall thickness was measured in transverse scans using the medial or lateral wall and including all identifiable layers. The anterior wall was excluded while in the near field of the ultrasound beam; the posterior wall was often obscured because of distal enhancement and acoustic shadowing cast by stones when present. Transverse measurements are subject to an error attributable to the ultrasound beam width. In this application, where the depth and echo intensity do not vary substantially between patients, the errors should be systematic for a given transducer or beam profile and so will not affect the reproducibility of the measurement.
2. Modification in wall reflectivity such as evidence of an echofree layer (Lowe *et al.*, 1980; Marchal *et al.*, 1979).
3. Gall-bladder distension: the AP diameter was measured in the widest section of the body or fundus, considering the fluid-filled lumen only.
4. Pain elicited by probe palpation over the gall-bladder area, the "echographic Murphy sign" (Taylor and Jacobson, 1980).

Cholecystosonography was always completed with examination of the entire upper abdomen, attention being paid to the liver, biliary ducts, pancreas and right kidney; free fluid in the peritoneum was sought.

RESULTS

One or more of the echographic signs considered were present in all patients investigated.

Wall thickness (Fig. 1).

Thickening of the wall ranging between 3 and 17 mm, was found in 36 patients (90%). In the most consistent group the wall measured from 5 to 7 mm; the mean value for all patients was 8.08 mm (Table I).

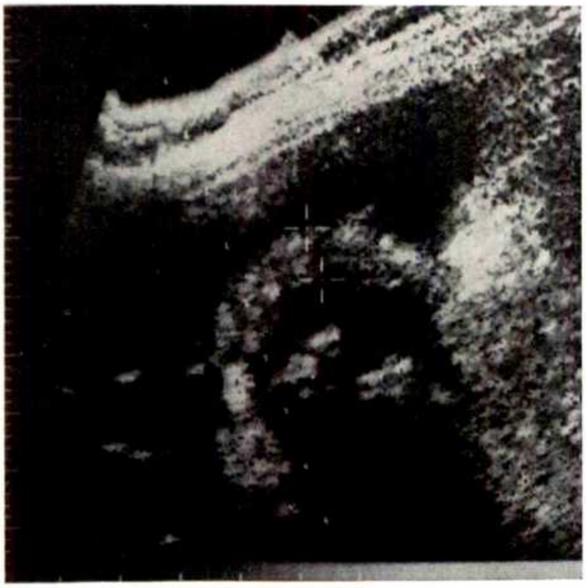
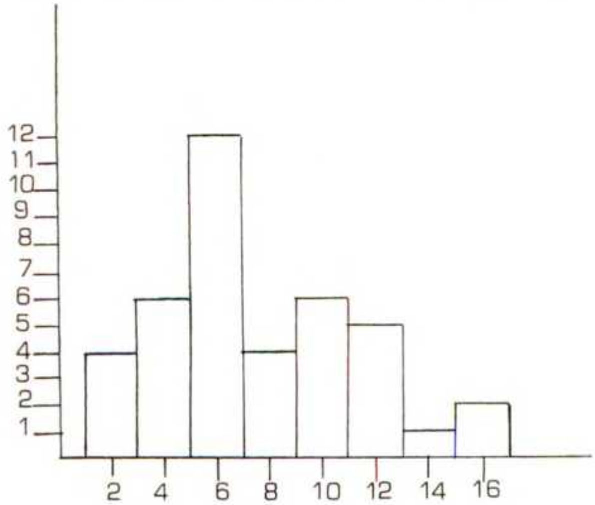


FIG. 1.

Acute cholecystitis with cholelithiasis. Transverse scan of the gall bladder shows a grossly thickened wall with relatively well-defined margin and irregularly reflective structure. Acoustic shadowing cast by stones prevents evaluation of the posterior wall.

TABLE I

HISTOGRAM SHOWS NUMBER OF PATIENTS (ORDINATES) IN RELATION TO GALL-BLADDER WALL THICKNESS (ABSCISSAE).



Ultrasonographic wall structure (Figs. 2, 3 and 4).

The thickened wall was generally hyperreflective with a poorly delineated outer margin. In 27 patients (67.5%) an echofree layer was noted within the

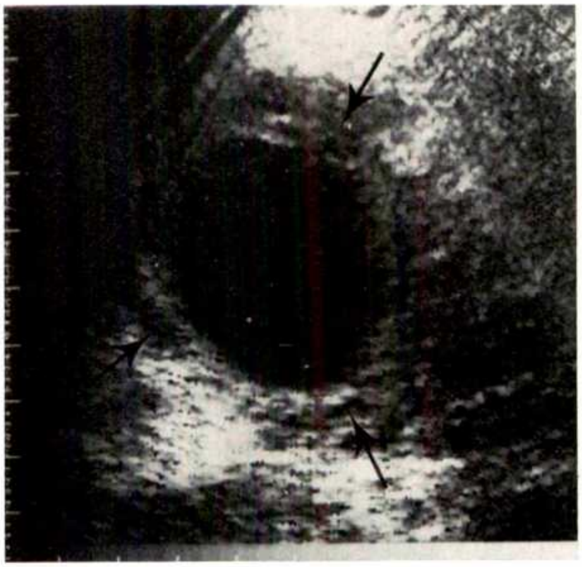


FIG. 2.

Acute cholecystitis. Transverse scan. Thickened, low reflectivity wall with ill-defined margin. An echofree layer (arrows) within the wall completely surrounds the lumen.

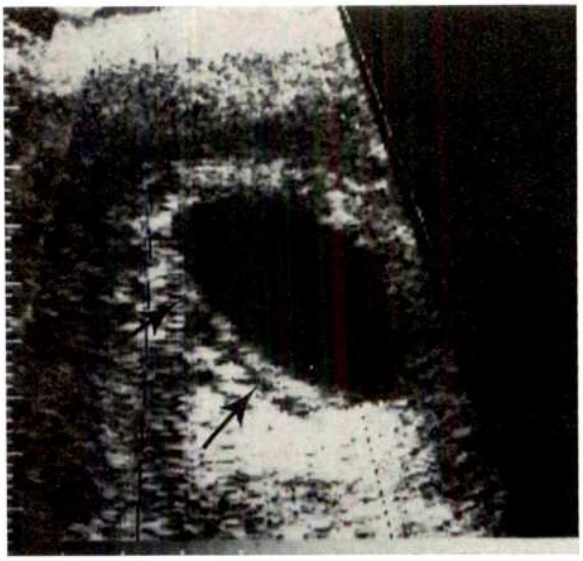


FIG. 3.

Acute cholecystitis. Longitudinal scan. Thick-walled gall bladder with ill-defined outer margin. An echofree layer (arrows) is seen only in a portion of the wall.

hyperechoic wall, which completely surrounded the lumen in 11 patients, and was more or less incomplete in the remaining 16. In four of these a second, incomplete echofree layer was also identifiable.

Gall-bladder distension

The mean value of the AP diameter was 3.72 cm and in 19 patients (47.5%) the lumen was larger than 4 cm.

Gall-bladder content

Thirty-three patients (82.5%) had cholelithiasis. In two cases the lumen was completely filled with small diffuse echogenic material which did not cause acoustical shadowing and was not gravity dependent. This pattern is thought to represent empyema (Fig. 5) or gangrenous cholecystitis (Kane, 1980).

Echographic Murphy sign

This sign was always present during the early stage of the disease, but with variable intensity.

The echographic signs alone permitted recognition of acute cholecystitis in 34 patients (85%): diagnosis was based on wall thickening, evidence of a sonolucent layer and a lumen greater than 4 cm, along with thick walls. In five patients we found cholelithiasis alone. In one patient the only detectable alteration was a slightly thickened wall.

DISCUSSION

Acute cholecystitis is in most cases a complication of cholelithiasis and usually presents as an abdominal emergency with typical clinical features and a long history of gall-bladder disease, though occasionally the clinical context can be equivocal and gall-stones may be absent, as in acalculous cholecystitis. Rapid, accurate imaging of the gall bladder is always desirable, since early surgical intervention is the most effective therapy (Dalmas *et al.*, 1979; Lennert and Siegmund, 1979).

Pathologically the gall-bladder wall is thickened because of oedema and inflammatory cellular infiltration which may, to a variable degree, extend to the adjacent liver parenchyma (Marchal *et al.*, 1978). Such alterations cannot be demonstrated by current radiological techniques (plain film abdominal radiography, oral cholecystography, intravenous cholangiography). Radionuclide cholescintigraphy depends on the presence of a stone obstructing the neck of the gall bladder or the cystic duct (Seltzer and Jones, 1980). Infusion tomography of the gall bladder has been suggested as a method of evaluating the gall-bladder wall (Dalla Palma *et al.*, 1978; Karp *et al.*, 1979; Moncada *et al.*, 1977); this procedure is time-consuming and unpleasant for the

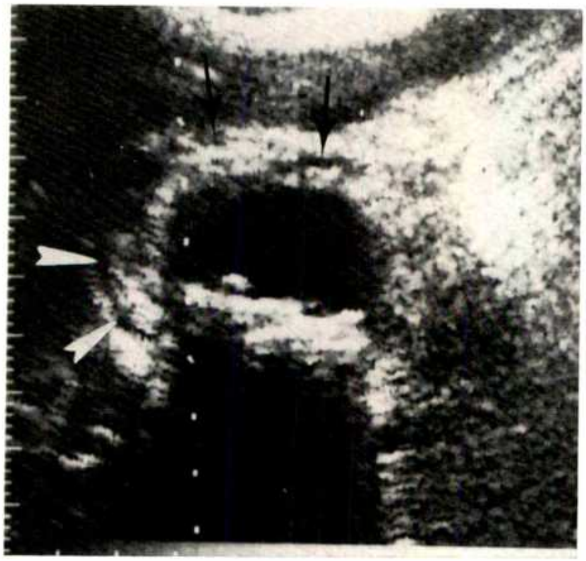


FIG. 4.

Acute cholecystitis with cholelithiasis. Transverse scan. Markedly thickened wall with several echofree layers (black and white arrows). Obvious acoustic shadowing obscures the posterior wall.

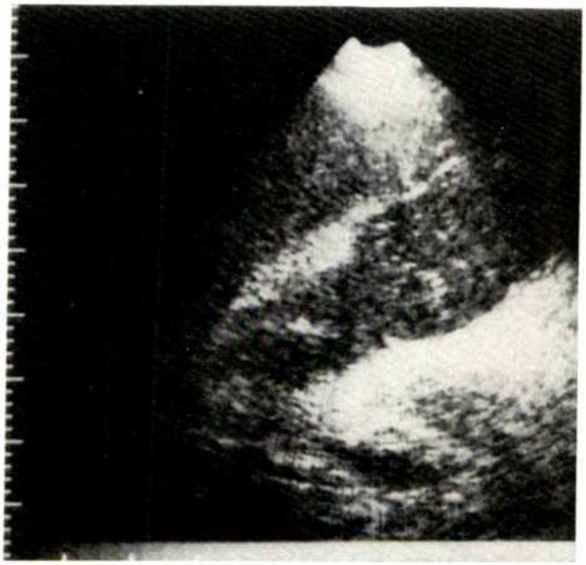


FIG. 5.

Empyema of the gall bladder. Longitudinal scan through a markedly enlarged gall bladder filled with small, diffuse, reflective material. Note the irregularly thickened wall.

UNIVERSITY COLLE LIBRARY

patient and there is evidence that it is subject to error (Handler, 1979). Experience with computed tomography with contrast enhancement, though limited, indicates that this technique is accurate in diagnosing acute cholecystitis (Solomon *et al.*, 1979). Its high costs and lack of availability will, however, restrict its use. Ultrasonography satisfies the clinical need for rapid gall-bladder visualization and reliable detection of disease. Ultrasound permits the recognition of wall alterations, the determination of the size of the gall bladder and the detection of calculi.

A hyperreflective gall-bladder wall with a thickness of more than 3 mm was found in 90% of patients in our study. Thickening can also be seen in a normal contracted gall bladder, in chronic cholecystitis, in cholelithiasis (Marchal *et al.*, 1979; Mindell and Ring, 1979; Weill, 1980), in ascites (Sanders, 1980) and in association with hypoalbuminaemia (Fiske *et al.*, 1980). Our experience suggests that thickening in these conditions is not as marked as in cholecystitis and is not associated with lumen distension. The clinical context is usually distinctive.

The presence of an echofree area within the gall-bladder wall is thought to be characteristic of acute cholecystitis and related to inflammatory oedema of the subserosa. This sign was evident in 67% of our patients with cholecystitis but we have also encountered it outside the study group in acute hepatitis (two cases) (Fig. 6), alcoholic cirrhosis (two cases) and in a patient with cholangitis. An echofree layer in the wall has been found after fatty meal or intravenous injection of cholecystokinin (Marchal *et al.*, 1980). In our experience this sign is much more frequently encountered in acute inflammation than in other conditions and when associated with other echographic signs and/or with clinical symptoms may truly be considered diagnostic.

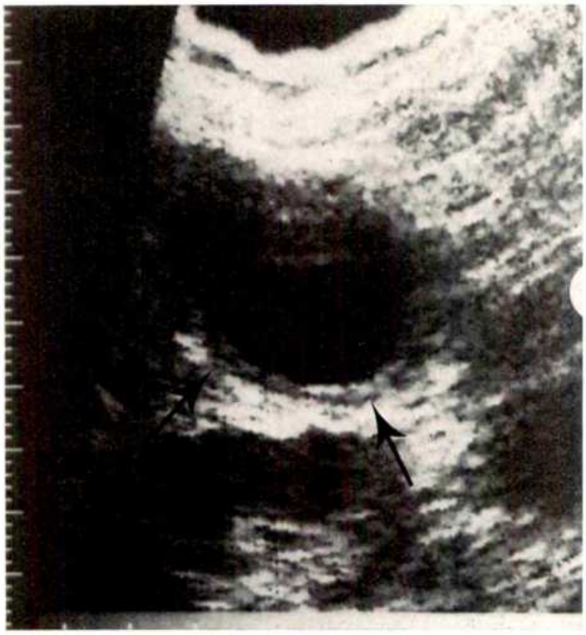


FIG. 6.

Sonogram of the gall bladder in acute hepatitis. Transverse scan. Moderate thickening of the wall with thin, echofree layer (arrows) along the posterior margin.

Non-specific signs of acute cholecystitis are distension of the gall bladder and cholelithiasis.

The significance of gall bladder sonographic dimensions is controversial: a width of up to 4 cm is considered normal by some investigators (Weill, 1980). This may be true when walls are normally thin; we feel that thick walls such as in cholecystitis may diminish the space occupied by the fluid content and therefore reduce the measurable lumen. Since a distended lumen may be the result of other pathological conditions or simply represent a normal variation, this sign is significant only when other echographic abnormalities are present.

Detection of gall-stones, although non-specific, has great practical significance when a clinical diagnosis needs confirmation and in patient management.

In five of our six echographic negatives for acute cholecystitis (where specific wall signs were absent) ultrasound demonstrated stones as a possible cause of the symptoms.

A positive Murphy sign could be recorded in practically all patients examined in the acute phase of the disease. This sign can be present in other forms of gall-bladder disease and in nearby inflammatory conditions: its intensity is subjective and quite variable. If the gall bladder is seen to be distorted by probe pressure at the time that pain is produced the reliability of this sign is enhanced (Finberg and Birnholz, 1979).

Ultrasound can also reveal complications of acute cholecystitis such as gangrenous necrosis and empyema or pericholecystic abscess formation (Bergman *et al.*, 1979; Kane, 1980). Whilst seven cases of empyema were found at surgery only two were diagnosed ultrasonically, therefore the echographic demonstration of uncomplicated cholecystitis cannot rule out empyema.

Ultrasound examination is valuable, even when negative for gall-bladder disease; in such cases a general survey of the upper abdomen may show other cause of symptoms, *e.g.* pancreatitis or renal abscess.

Conclusion

Ultrasound is recommended as the first investigation for patients presenting with clinically suspected acute cholecystitis; it will often be the only radiological investigation before surgery.

The safeness and rapidity of ultrasound examination play a determining role for acutely ill patients, when a quick decision must be taken regarding surgery.

Ultrasound permits a confident diagnosis of acute cholecystitis, showing wall alterations due to the inflammatory process in the majority of cases (85% of our patients).

Cholelithiasis is usually evident when associated and it may be the only echographic sign of the disease if parietal alterations are absent (12.5% of our patients). Detection of gall-stones is in any case important to support a clinical diagnosis.

In only one of our 40 patients with surgically proven acute cholecystitis was ultrasound examination negative for gall-bladder disease.

REFERENCES

Bergman, A. B., Neiman, H. L. and Kraut, B., 1979. Ultrasonic evaluation of pericholecystic abscess. *American Journal of Roentgenology*, *132*, 201–203.

Dalla-Palma, L. D., Bazzocchi, M. and Di Pietrantonio, M., 1978. Abdominal contrast tomography in the evaluation of the gall bladder and biliary tract (with emphasis upon jaundiced patients). *British Journal of Radiology*, *51*, 484–493.

Dalmas, M., Picaud, R., Anfossi, G. and Guidicelli, G., 1979. Les cholecystites aigues lithiasiques. *Journal de Chirurgie*, *116*, 193–200.

Engel, J. M., Deitch, E. A. and Sikkema, W., 1980. Gall-bladder wall thickness: sonographic accuracy and relation to disease. *American Journal of Roentgenology*, *134*, 907–909.

Finberg, H. J. and Birnholz, J. C., 1979. Ultrasound evaluation of the gall-bladder wall. *Radiology*, *133*, 693–698.

Fiske, C. E., Laing, F. C. and Brown, T. W., 1980. Ultrasonographic evidence of gall-bladder wall thickening in association with hypoalbuminaemia. *Radiology*, *135*, 713–716.

Handler, S. J., 1979. Ultrasound of gall-bladder wall thickening and its relation to cholecystititis. *American Journal of Roentgenology*, *132*, 581–585.

Jacobson, P. and Taylor, K. J. W., 1980. Biliary system. In *Manual of Ultrasonography*. Ed. by K. J. W. Taylor *et al.* (Churchill Livingstone, New York), pp. 121–123.

Kane, R. A., 1980. Ultrasonographic diagnosis of gangrenous cholecystitis and empyema of the gallbladder. *Radiology*, *134*, 191–194.

Karp, W., Herlin, P., Holmin, T. and Owman, T., 1979. Infusion tomography and ultrasonography of the gall bladder in the diagnosis of acute cholecystitis. *Gastro-intestinal Radiology*, *4*, 253–261.

Lennert, K. A. and Siegmund, G., 1979. L'intervento precoce nella colecistite ecuta. *Minerva Chirurgica*, *34*, 837–842.

Lowe, S., Joseph, A. E. A. and Tungekhar, R., 1980. Double wall sign: a characteristic ultrasound appearance in acute cholecystitis. Proceedings of the British Medical Ultrasound Society, 12th Annual Meeting, Nottingham (unpublished abstract).

Marchal, G. J. F., Casaer, M., Baert, A. L., Goddeeris, P. G., Kerremans, R. and Fevery, J., 1979. Gall-bladder wall sonolucency in acute cholecystitis. *Radiology*, *133*, 429–433.

Marchal, G. J. F., Crolla, D., Baert, A. L., Fevery, J. and Kerremans, R., 1978. Gall-bladder wall thickening: a new sign of gall-bladder disease visualized by grey scale ultrasonography. *Journal of Clinical Ultrasound*, *6*, 177–179.

Marchal, G. J. F., Van de Voorde, P., Van de Voorde, W., Ponette, E. and Baert, A., 1980. Ultrasonic appearance of the filled and contracted normal gall bladder. *Journal of Clinical Ultrasound*, *8*, 439–442.

Mindell, H. J. and Ring, B. A., 1979. Gall-bladder wall thickening: ultrasonic findings. *Radiology*, *133*, 699–701.

Moncada, R., Cardoso, M., Danley, R., Rodriguez, J., Kimura, J. and Brandly, J., 1977. Acute cholecystitis: 137 patients studied by infusion tomography of the gall bladder. *American Journal of Roentgenology*, *129*, 583–585.

Sanders, R. C., 1980. The significance of sonographic gall-bladder wall thickening. *Journal of Clinical Ultrasound*, *8*, 143–146.

Seltzer, S. E. and Jones, B., 1980. Imaging the hepato-biliary-system in acute disease. *American Journal of Roentgenology*, *135*, 407–416.

Solomon, A., Kreel, L. and Pinto, D., 1979. Contrast computed tomography in the diagnosis of acute cholecystitis. *Journal of Computer Assisted Tomography*, *3*, 585–588.

Weill, F. S., 1980. Cholelithiasis and cholecystitis. In *Ultrasononography of Digestive Disease*. Ed. by F. S. Weill (C. V. Mosby Co., St. Louis), pp. 257–263.

1981, *British Journal of Radiology*, *54*, 932–938

Diaphyseal osteosarcoma

By *J. M. Haworth, M.B., B.S., *I. Watt, M.R.C.P., F.R.C.R., †W. M. Park, D.M.R.D., F.R.C.R and *J. Roylance, D.M.R.D., F.R.C.R.

Departments of Radiology, *Bristol Royal Infirmary, Bristol and
†The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, Salop

(*Received June 1981*)

ABSTRACT

Fifteen cases of diaphyseal osteosarcomas were found in a review of 157 cases of long bone osteosarcoma (9.5%) and two further examples were added. The clinical and histological features of the diaphyseal osteosarcomas were indistinguishable from those of the commoner juxta metaphyseal osteosarcomas. The radiological features, however, fell into four distinct patterns: Group I had the classical appearance of a conventional osteosarcoma; Group II showed dense cortical sclerosis with bony expansion but no soft tissue swelling or break of the cortex at presentation; Group III presented with a pathological fracture through a purely osteolytic lesion; Group IV usually had the classical appearances of an osteosarcoma in the diaphysis but had, in addition, dense separate sclerotic lesions which were proximal to the tumour in the humerus and distal to it in the femur. The importance of these four groups lies in the quite distinct differential diagnosis which each presents.

The usual site for an osteosarcoma in a long bone is close to the metaphysis and in that site there is little difficulty in radiological diagnosis (Ross, 1964). Osteosarcoma occurs, however, in the diaphysis where it may cause considerable diagnostic difficulty which has not been previously emphasized. Seventeen examples of diaphyseal osteosarcoma occurring in previously normal long bone have been reviewed to evaluate the specific radiological, clinical and pathological features of these tumours.

PATIENTS AND METHODS

All 157 patients with long bone osteosarcoma, consecutively classified by the Bristol Bone Tumour Registry over a 26-year period, have been reviewed. The distance of the centre of the tumour from the end of the bone was expressed as a percentage of the length of the bone involved. Tumours occurring in the middle 40% of the bone length were classified as diaphyseal (Fig. 1) and were reviewed in detail. Two further cases were added from the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry.

RESULTS

The location of the tumours in the 157 cases from the Bristol Bone Tumour Registry conformed with the recognized pattern and were commonest in the distal femur, followed by the proximal tibia and then the proximal humerus (Fig. 2). There were 15 cases of diaphyseal osteosarcoma (9.5%). There was no

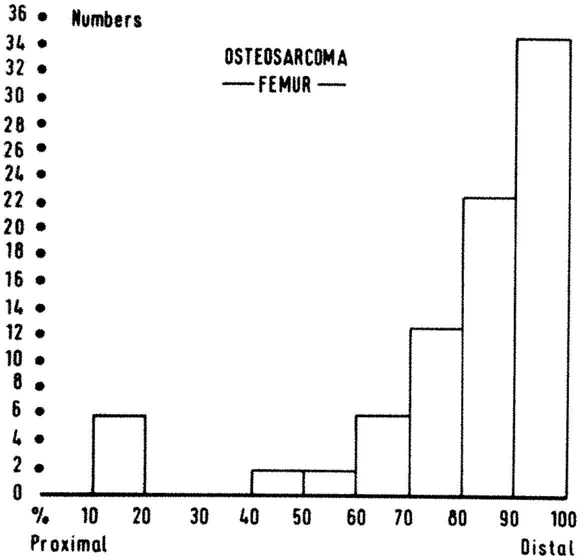


FIG. 1.

Histograms showing the distribution of osteosarcoma arising in the femur amongst the 157 long bone osteosarcomas from the Bristol Bone Tumour Registry.

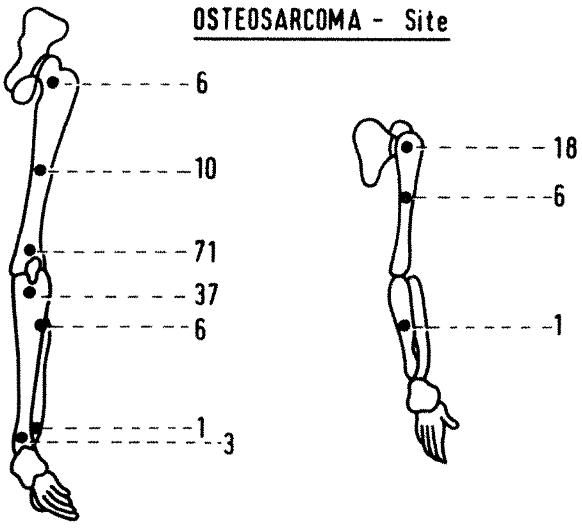


FIG. 2.

Diagram showing the number of long bone sarcomas occurring in each site. 157 Bristol Bone Tumour Registry cases and two diaphyseal lesions from Oswestry.

difference in the age or sex incidence of diaphyseal and juxta metaphyseal osteosarcoma (Fig. 3).

Of the 15 patients from the Bristol Bone Tumour Registry and the two additional patients, ten lesions occurred in the femur (7 females/3 males) with an age range of nine to 71 years, mean of 21.4 years. Six lesions occurred in the humerus (two females/four males) with an age range of 15 to 59 years, mean 28.3 years. One lesion occurred in the ulna of a 16-year-old girl.

The histological findings in the diaphyseal group did not differ from those of conventional osteosarcomas, being of a mixed pattern with a predominantly osteoblastic, chondroblastic, fibroblastic or anaplastic character. The five-year survival rate of the diaphyseal osteosarcomas was 23%, similar to that of all osteosarcomas (Lee, 1975).

All patients presented with pain and swelling, the longest history of symptoms being two years, the shortest being only five weeks. In three cases the presenting feature was a spontaneous fracture.

RADIOLOGICAL FEATURES

The presenting radiological appearances of diaphyseal osteosarcomas had four distinct patterns.

Group I (Typical osteosarcoma)

The tumours in this group showed mixed osteosclerosis and osteolysis, with elevation of the periosteum forming Codman's triangles. The cortex was

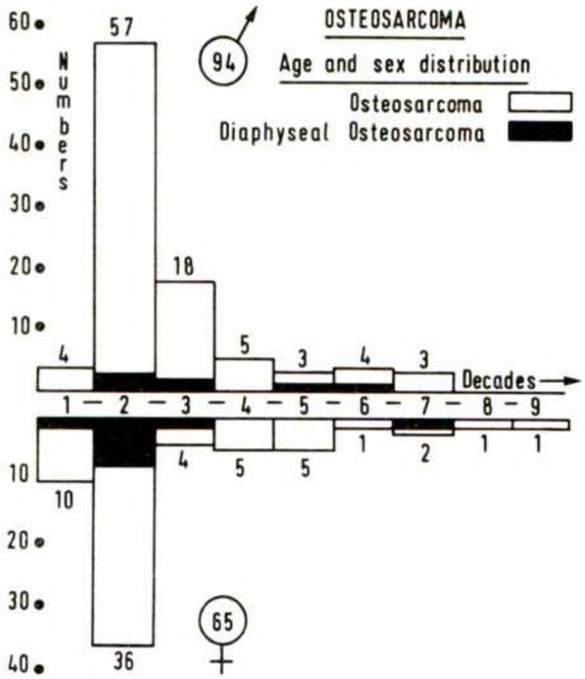


FIG. 3.

The age and sex distribution of all long bone osteosarcomas and diaphyseal osteosarcomas from 157 cases from the Bristol Bone Tumour Registry and two diaphyseal osteosarcomas from Oswestry.

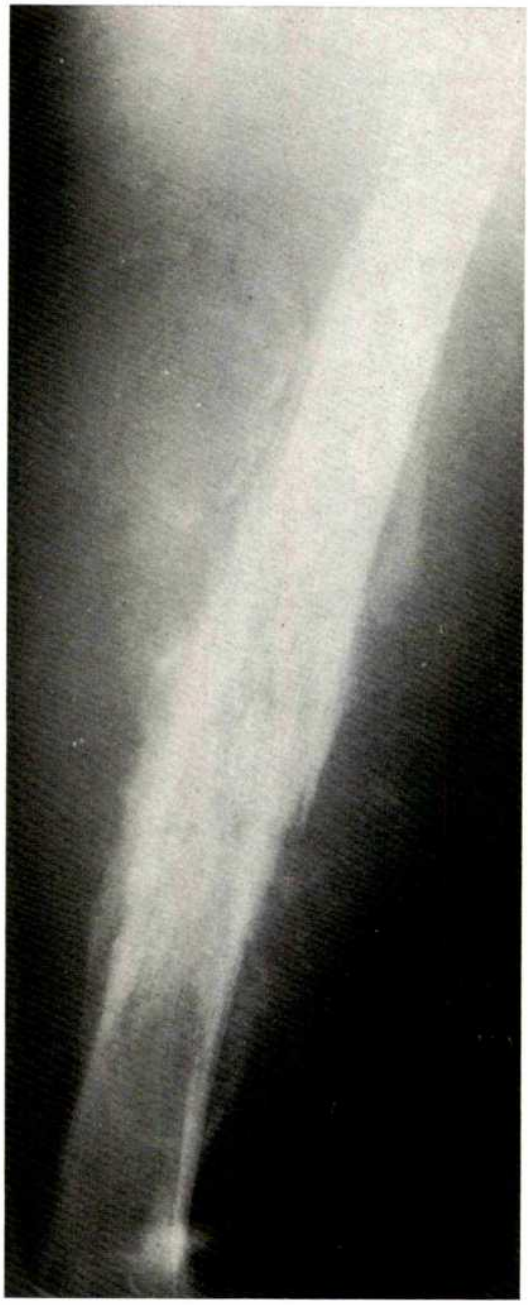


FIG. 4. *Type I.*

Diaphyseal osteosarcoma of the femur. Extensive areas of bone destruction and sclerosis are shown with well-marked Codman's triangles, tumour bone formation and a soft tissue mass.

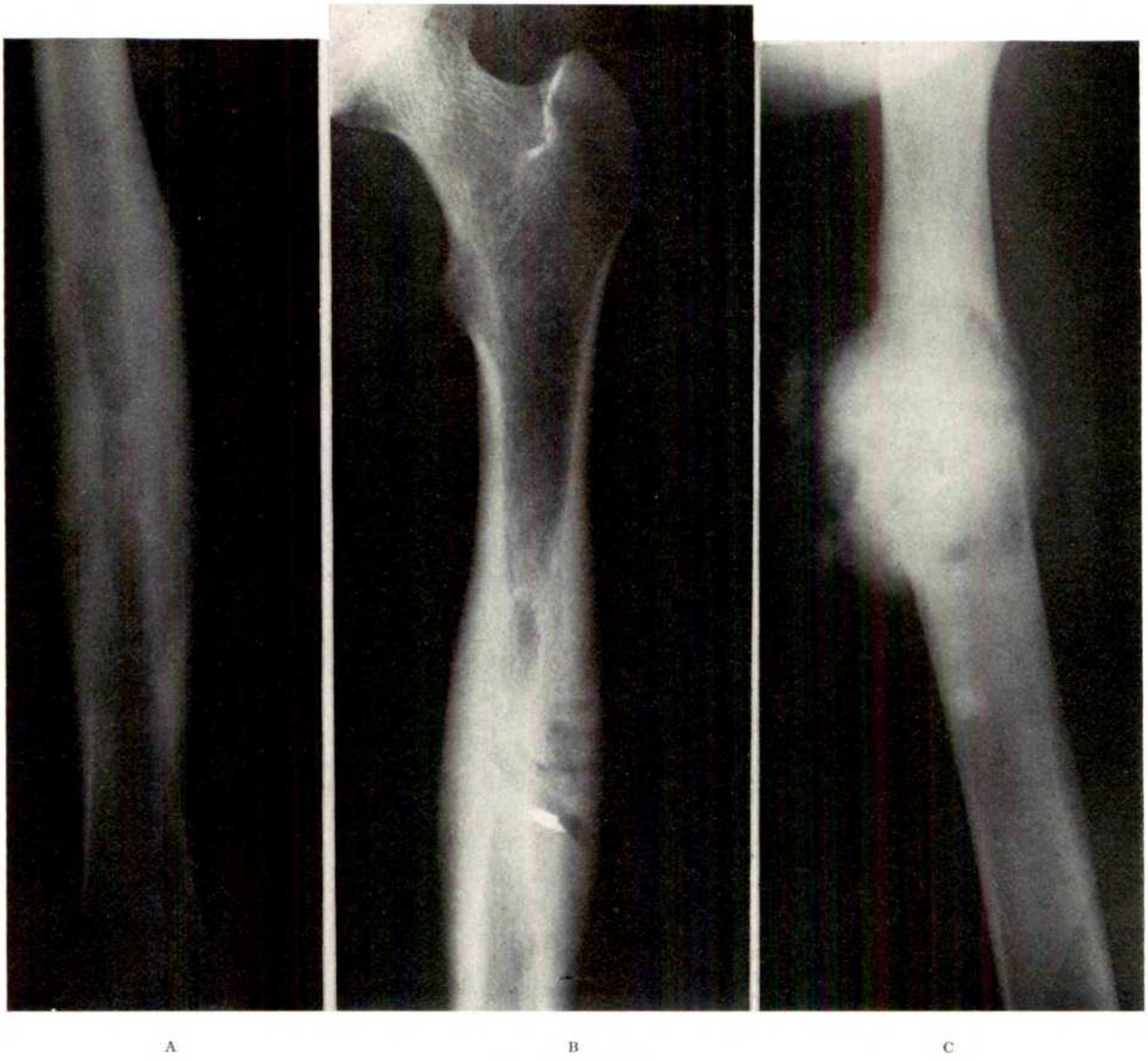


Fig. 5. *Type II.*

(a) Diaphyseal osteosarcoma at presentation. There is fusiform cortical expansion, no evidence of bone destruction or periosteal reaction.

(b) The same lesion two years later following several bone biopsies during which the tip of the biopsy drill was broken.

(c) Two years later there is now extensive bone destruction and bone production, extending into the soft tissues with cortical destruction.

breached with surrounding well-defined soft-tissue swelling (Fig. 4). An arteriogram of a lesion in the ulna revealed typical arterial abnormalities with tumour blush and early venous drainage (Voegeli and Fuchs, 1976).

There were six cases in this group, five females and one male, with an age range of 12 to 61 years, mean of 22.8 years. Three of the lesions were in the femur, two in the humerus and one in the ulna. Of the six patients, two remain alive and apparently disease free at five and ten years from presentation. Another patient is of recent presentation. Three have died after six months, two years and five years with pulmonary metastases.

Group II (Atypical sclerotic)

The radiological features were those of a dense sclerotic lesion expanding the bone with little or no separate periosteal reaction (Fig. 5a). All lesions were situated in the femoral diaphysis. There were three

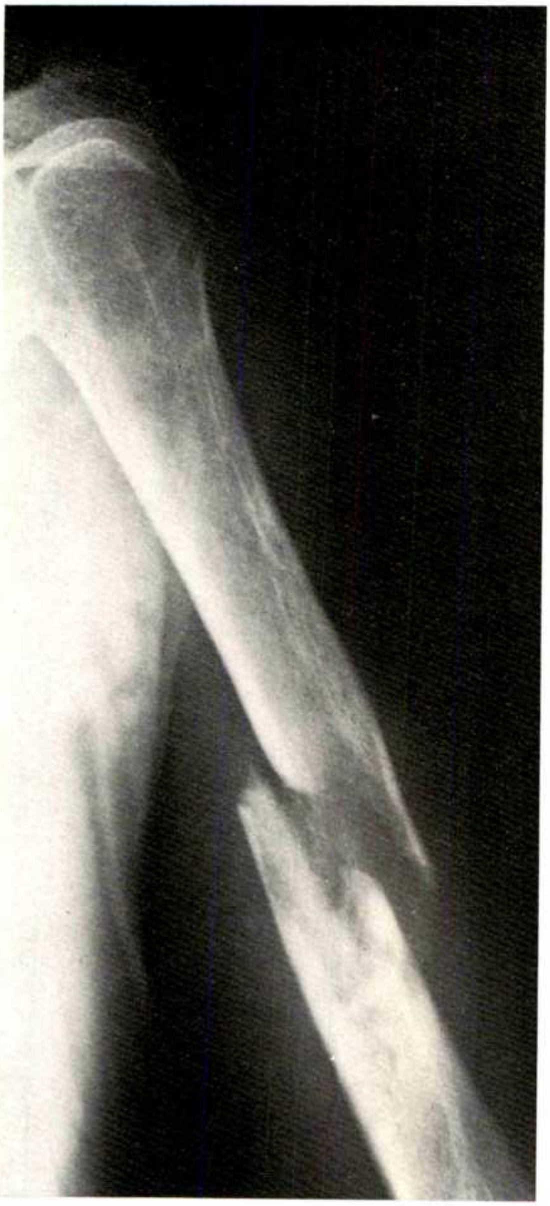


FIG. 6. *Type III.*

Diaphyseal osteosarcoma at presentation. There is an ill-defined purely osteolytic lesion in the mid-shaft of the humerus with a pathological fracture. There is no sclerosis or periosteal new bone formation.

cases in this group, two females and one male, with an age range of 11 to 19 years, mean of 15.3 years. All have died: one, two and seven years from presentation, giving a mean survival of 3.3 years.

In one patient the lesion remained radiologically unchanged for a period of two years, during which two inconclusive biopsies were performed. At one biopsy the lesion was so hard that it broke the tip of the biopsy drill (Fig. 5B). A third biopsy two years later showed the lesion to be an osteosarcoma and at this stage the radiological appearances had changed with breaching of the cortex and soft tissue extension of the tumour (Fig. 5C). The patient remained disease free for five years after amputation but died with pulmonary metastases in the sixth year.

Group III (Atypical destructive)

These presented with pathological fractures through purely osteolytic, ill-defined lesions. There was no bone expansion, evidence of periosteal new bone, sclerotic reaction or soft tissue extension of the tumour (Fig. 6). There were three cases, one female and two males, with an age range of nine to 59 years, mean of 37.3 years. Two of the tumours involved the humerus and one the femur. Two cases have died at two and four years from presentation; one case is of only recent presentation.

Group IV (Diaphyseal osteosarcoma with remote intraosseous sclerotic lesions)

There were five cases in this group, three males and two females, with an age range of 16 to 29 years, mean 21 years. Three of the primary tumours were in the femur and two in the humerus.

All the primary lesions showed both bone production and bone destruction. In four there was periosteal elevation with Codman's triangles and soft tissue extension of the tumour, with sunray spiculation in three. One case demonstrated neither periosteal reaction nor soft tissue extension of the tumour but had a discrete cortical fracture through the lateral aspect of the diaphyseal tumour (Fig. 7). Multiple, dense, well-defined sclerotic lesions were seen at presentation in all, and in four were separated from the main diaphyseal lesion by radiologically normal bone (Fig. 8). The sclerotic lesions were larger, denser and better-defined the further they were situated from the diaphyseal lesion. The lesions were proximal to the primary lesion in the humerus and distal to the primary lesion in the femur. In two cases the largest, most dense and best defined lesion was situated in the epiphysis.

Arteriography in one (Haworth *et al.*, 1979) demonstrated a very vascular tumour in the mid shaft of the humerus with a pathological circulation and a tumour blush. There was minimal hypervascularity in the region of the dense sclerotic lesions. A $^{99}\mathrm{Tc^m}$ methylene diphosphonate scan showed some increased uptake in the region of the diaphyseal lesion but marked uptake in the region of the sclerotic lesions. There was also some increased uptake in the intervening shaft. Histologically the entire humeral shaft was involved by the tumour. The area corresponding to the diaphyseal lesion was mainly necrotic and the sclerotic lesions contained the most active osteosarcoma.

Four patients have died with pulmonary metastases at three, seven, 12 and 15 months from presentation. One is alive at 42 months with probable but unconfirmed pulmonary metastases.

DISCUSSION

The success currently being achieved by advances in chemotherapy in the management of osteosarcoma has greatly increased the importance of early diagnosis. Such a diagnosis is traditionally established by the histopathological appearances and more recently also by cytological and histochemical means. The interpretation of the microscopic findings demands close correlation with the radiological features. The radiologist must, therefore, ensure that a full radiological assessment is made available to the histologist. The essential prerequisite to this assessment is the correct interpretation of the initial plain films.

Each of the four groups of plain film appearances of diaphyseal osteosarcoma presents separate problems in diagnosis or management.

The lesions in Group I exhibit typical radiological features of an osteosarcoma (Ross, 1964; Dahlin and Coventry, 1967; Dahlin, 1978) but their atypical site may deter the correct interpretation and encourage the diagnosis of a malignant round cell tumour.

The dense expansile lesions in Group II provide a particularly difficult diagnostic problem because there is no immediate impression of malignancy. The benign appearance undoubtedly delayed the diagnosis in all cases and may have adversely affected the ultimate prognosis. The initial radiographic differential diagnosis may include chronic osteomyelitis, previous trauma, or a benign osteoblastic tumour. It is possible that these osteosarcomas arose in pre-existing benign lesions, and the initial slow evolution (Fig. 5A–C) supports this concept. However no histopathological evidence of such a lesion could be detected in any case.

In Group III, with purely osteolytic lesions presenting with a pathological fracture, the presence of a malignant lesion was correctly inferred in all cases. The exact diagnosis was unclear however and differential diagnosis of this variety included metastasis, fibrosarcoma, and reticulum cell sarcoma.

The Group IV lesions, presenting with separate dense sclerotic opacities, have a different importance. In most the mid-shaft lesion has the typical radiological features of an osteosarcoma, so that the

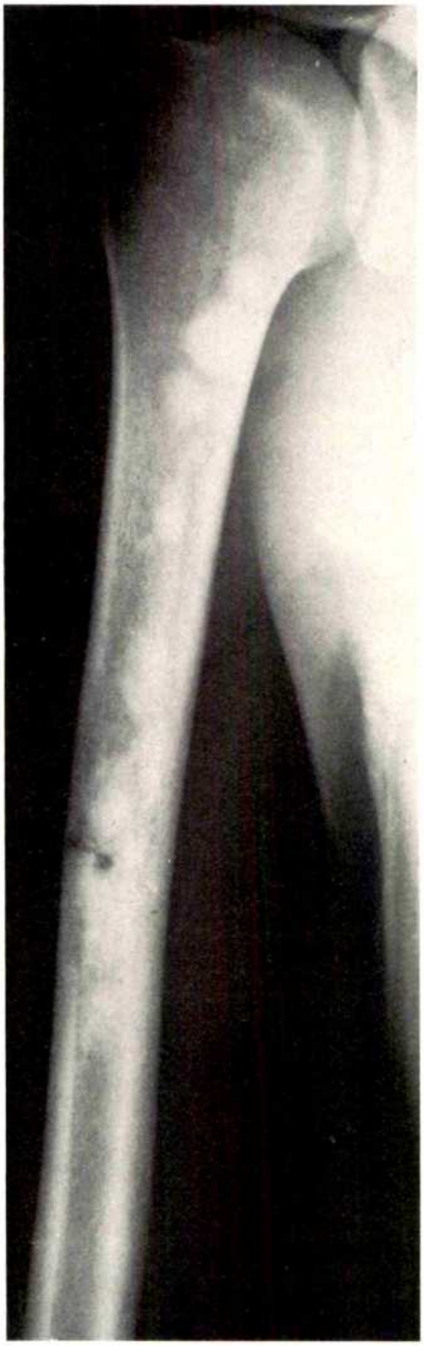


FIG. 7. *Type IV.*

Diaphyseal osteosarcoma of the humerus. Localized fracture of the mid-shaft with a discrete area of bone destruction, and extensive surrounding medullary sclerosis. No periosteal reaction or soft tissue mass. There are several dense rounded sclerotic opacities extending proximally in the medullary cavity each with a narrow zone of surrounding translucency. The most proximal lesions are the largest.

diagnosis should not be in doubt. The separate dense sclerotic lesions have a unique appearance and distribution and once their association with osteosarcoma is appreciated they should be readily recognized. Angiographically the lesion is most abnormal in the osteolytic diaphyseal component whereas scintigraphy shows most uptake in the sclerotic lesions of the metaphysis and epiphysis (Haworth *et al.*, 1979). Biopsy in the most angiographically abnormal site will provide suitable material to make an unequivocal diagnosis of malignancy (Viamonte *et al.*, 1973). However, material from the sites with the highest uptake of radionuclide, corresponding to the sclerotic medullary component, may offer the most tumour specific histopathology.

It is of interest to note that the location of the dense sclerotic lesions corresponds to the commonest sites of primary osteosarcomas in both the humerus and the femur. The sclerotic lesions are also larger and more dense in the region of the proximal humerus and the distal femur where inherent bone turnover is at its greatest. An as yet undefined local factor may provide a stimulus for the rapid evolution of osteosarcoma cells. Although these lesions are macroscopically discrete, histologically the intervening medulla is replaced by tumour, and the sarcomatous involvement is much more extensive than may be at first suggested.

Once the four presenting patterns of diaphyseal osteosarcoma have been appreciated it is possible to suspect the diagnosis from the initial plain

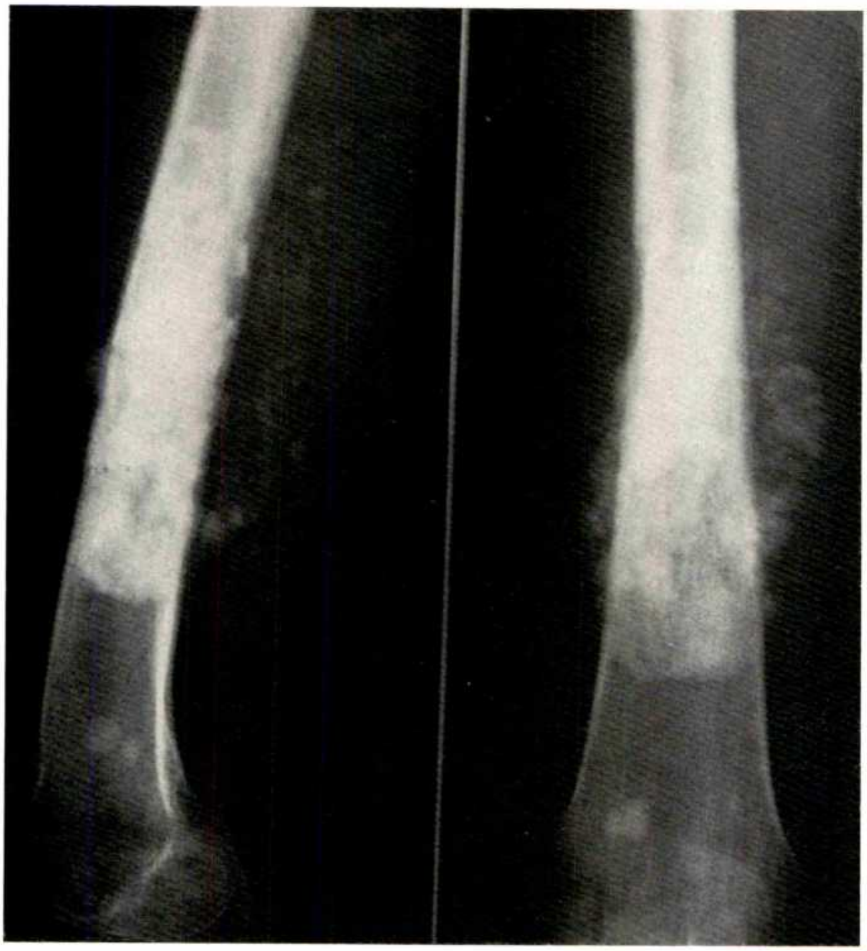


FIG. 8. *Type IV*.

Diaphyseal osteosarcoma of the femur with several dense sclerotic opacities extending distally in the medulla.

radiographs. This should lead to an urgent full radiological assessment including local tailored views, simple and computed tomography, chest films, skeletal scintigraphy and angiography followed by adequate biopsy. The accurate diagnosis and staging of the tumour thus established will facilitate immediate appropriate therapy.

ACKNOWLEDGMENTS

The authors wish to acknowledge the assistance given by the Bristol Bone Tumour Registry and in particular Dr. N. Sanerkin for reviewing the histology of the diaphyseal osteosarcomas. They would also like to thank Mr. E. J. Turnbull for the drawings for Figs. 1, 2 and 3 and Mr. J. Hancock for preparation of the prints.

REFERENCES

DAHLIN, D. C., 1978. *Bone Tumours*, 3rd edit. (Charles C. Thomas, Springfield, Illinois).

DAHLIN, D. C. and COVENTRY, M. B., 1967. Osteogenic sarcoma. A study of 600 cases. *Journal of Bone and Joint Surgery*, *49A*, 101–110.

HAWORTH, J. M., MCCALL, I. W., PARK, W. M. and WATT, I., 1979. Sclerotic medullary spread in diaphyseal osteosarcoma. *Skeletal Radiology*, *4*, 212–215.

LEE, E. S., 1975. Osteosarcoma: a reconnaissance. *Clinical Radiology*, *26*, 5–25.

ROSS, F. G. M., 1964. Osteogenic sarcoma. *British Journal of Radiology*, *37*, 259–276.

VIAMONTE, M., ROSEN, S. and LE PAGE, J., 1973. Non-specifity of abnormal vascularity in the angiographic diagnosis of malignant neoplasms. *Radiology*, *106*, 59–63.

VOEGELI, E. and FUCHS, W. A., 1976. Arteriography in bone tumours. *British Journal of Radiology*, *49*, 407–415.

Book reviews

Bone Metastases. Ed. by L. Weiss and H. A. Gilbert, pp. xxiv+512, 1981 (G. K. Hall, Boston, Mass.), $55.00 (+15% outside USA).
ISBN 0-8161-2129-X

This is the fourth volume of a Monograph Series on the subject of metastases. Previous works covered pulmonary, brain and lymphatic deposits and a fifth on liver metastases is in preparation.

"Bone Metastases" is an important publication bringing together the facts and theories associated with the metastatic processes involved in the development of deposits in bone. The first part ranges from the concept of cell shedding by tumours based on the physical and biochemical processes involved, through the various pathways of anatomical spread, to the mechanisms involved in bone destruction by tumour cells. It also covers the consequences of metastatic disease in bone, in terms of the biochemical upset and related symptomatology for the host. There is also a particularly interesting chapter on the resistance of cartilage to invasion by tumour. The second part covers the methods of diagnosis of metastatic bone disease, commencing with pathology. There are valuable data from post-mortem statistics of the incidence of metastatic disease in various parts of the skeleton as well as the behaviour of primary tumours spreading to bone. Consideration is given to the relative merits of biopsy, large-bone needling and fine needle aspiration for cytology. This section is well illustrated by black and white photomicrographs which are well produced.

There is an excellent radiological section not only indicating the methods available to help establish the diagnosis but also relating the likelihood of each diagnosis to sex, age, site and appearances. This section is illustrated very fully with an excellent series of radiographs well reproduced. There follows a chapter on radionuclide scanning and views are expressed on the value of computed tomography, again with a number of illustrations.

The management of the patient with metastatic disease in bone is covered from the viewpoint of orthopaedic surgery, rehabilitation, control of pain and the possible roles played by prostaglandins. There is also a large section on the chemotherapy of patients with metastases. This starts with a detailed account of pharmacokinetics and distribution studies of adriamycin, through to the results of the use of single and multiple agents used in attempts to control bone metastases from various cancers. There is a particularly useful account of the place of hormone therapy in the managementof bone metastases, supported by tables of the results of many clinical trials. Finally, as radiation therapy plays such an important role in the management of these patients, there is a large section devoted to this aspect. It covers not only localized radiations but the more recent concept of wide-field therapy together with results and associated side effects. For localized treatments the results of various dosages and fractionation schemes are presented. This section concludes with an account of the tolerance of bone to radiation.

The whole work is well indexed by subject and author and is an important contribution to medicine.

BRENDAN HALE.

Cahiers de Radiologie. 2. Le crâne. By D. Doyon and J. P. Monnier, pp. 80+iv, 1981 (Masson, Paris).
ISBN 2-225-68090-6

This is the second in a projected series of ten pictorial volumes designed to complement standard French radiological textbooks. Text is reduced to a minimum, the 80 pages being devoted almost entirely to reasonably high-quality images of skull radiographs, CT, angiography, etc.; although the title suggests that the skull is the only subject of the book, its contents are also considered.

It would be easy to find fault with this slim volume, in terms particularly of omission of important diseases, unbalanced emphasis and incorrect criteria for assessing correct radiographic positioning. I personally do not like the fold-out numerical key sheet at the end, emulating, I presume, George du Boulay's book on the skull (which makes the latter's omission from the bibliography doubly curious), only here applicable to virtually all the figures. Having said that, one's more forceful impression is that this is a rather useful and well produced survey of a field of radiological expertise which, in the CT era, is in great danger of being neglected.

The size of the book has been kept to a minimum "to render it accessible to students". Although the verbal content is simple enough for most anglophones, its price here may well render it somewhat less accessible.

T. MOSELEY.

1981, *British Journal of Radiology*, *54*, 939–943 NOVEMBER 1981

The chest radiograph in leptospirosis in Jamaica

By *R. E. J. Lee, B.Sc., F.R.C.R., †S. I. Terry, D.T.M. & H., M.R.C.P. (U.K.),
*T. M. Walker, M.B., F.R.C.R., and ‡A. E. Urquhart, B.Sc., D.M.D.

Departments of *Radiology, †Medicine and ‡Pathology, University of the West Indies, Mona, Kingston 7, Jamaica

(*Received March 1981 and in revised form June 1981*)

ABSTRACT

A consecutive series of 44 patients with proven leptospirosis was studied to document the radiographic pulmonary abnormalities, assess their prevalence, correlate them with the clinical signs and symptoms and determine their prognostic significance. Abnormalities were found in ten patients (23%), this prevalence being less than previously noted. The abnormalities shown were non-segmental opacification (consolidation—eight cases), basal linear opacities (collapse—five cases) and pleural effusions (four cases). The first radiographic demonstration of a large pleural effusion in leptospirosis is recorded. Non-jaundiced patients had a higher prevalence (43%) of these abnormalities than jaundiced (13%). No other correlation with clinical signs or symptoms was found. The presence of these abnormalities had no prognostic significance.

It is concluded that the presence of radiographic pulmonary abnormality in in-patients with leptospirosis is common. These abnormalities are non-specific and can mimic other diseases leading to diagnostic difficulty. Such abnormalities may be extensive in the absence of clinical signs and symptoms.

Leptospirosis is a disease caused by spirochaetes of the genus *Leptospira*. It has a world-wide distribution (Cruickshank *et al.*, 1976; Spink, 1978) and is common in the tropics and in the developing countries. The clinical picture varies from mild constitutional upset to classical Weil's disease with fever, jaundice, haemorrhagic episodes, aseptic meningitis, hepatitis and nephritis. There are numerous serotypes but no specific clinical syndrome has been attributed to any of them.

Pulmonary involvement occurs and takes the form of haemorrhagic pneumonitis and, rarely, frank pulmonary haemorrhage (Burke *et al.*, 1976; Ch'iu and Liu, 1959; Havens *et al.*, 1941; Moeschlin, 1943). Few descriptions of the radiographic appearances of these lesions have appeared in the English literature (Nery *et al.*, 1977; Poh and Soh, 1970; Silverstein, 1953; Wang *et al.*, 1965). The discovery of extensive radiographic pulmonary abnormality in a patient with leptospirosis may present a difficult diagnostic problem. The prognostic significance of these abnormalities is not clear although some studies have suggested that their extent is proportional to the clinical severity of the disease (Wang *et al.*, 1965). Conflicting evidence also exists about the prevalence of these findings with reports of 40% (Research Laboratory of the Sino-Soviet Friendship Hospital, 1959), 33% (Nery *et al.*, 1977) and 67% (Wang *et al.*, 1965). The prevalence of pulmonary radiographic abnormalities in jaundiced patients has been found to be twice that in the non-jaundiced (Research Laboratory of the Sino-Soviet Friendship Hospital, 1959), but Wang *et al.* (1965) found a high prevalence (67%) in non-jaundiced patients.

A consecutive series of patients with proven leptospirosis was studied to document the radiographic pulmonary abnormalities, assess their prevalence, correlate them with the clinical signs and symptoms and determine their prognostic significance.

MATERIALS AND METHODS

All patients with leptospirosis treated at the University Hospital of the West Indies between January 1972 and December 1978 were reviewed. Ten patients with abnormal chest films were found in a total of 44 patients with chest films taken during the acute phase of their disease. (Table I). A further seven patients with abnormal chest films were excluded because they were suffering from co-existing diseases which produce chest film abnormalities—klebsiella (2) and pneumococcal pneumonia (1), staphylococcal lung abcess (1), recent thoracotomy (1) and acute renal failure (2). A further 61 patients with leptospirosis were seen during this period but were not X-rayed.

The diagnostic criteria for leptospirosis were: (a) identification of leptospiral spirochaetes on dark-ground microscopy; or (b) an agglutination titre of

TABLE I

GENERAL DETAILS OF PATIENTS

Chest radiograph	Male	Female	Age in years range and mean
Abnormal	7	3	3–68 (49)
Normal	27	7	5–81 (39)
Total	34	10	3–81 (41)

Present addresses: R. E. J. Lee: Department of Radiology, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP; T. M. Walker: Department of Radiology, Royal Berkshire Hospital, London Road, Reading, Berks.

1:100 or greater and/or a four-fold change in titre in successive studies.

Two patients were diagnosed on microscopy alone. The others had the following serotypes: *L. icterohaemorrhagiae* (three cases), *L. jules* (four cases), and *L. canicola* (one case). Those with normal films showed the same serotypes but with *L. abramis*, *L. patoc* and *L. pomona* in addition.

Results

The commonest abnormality (Table II) was non-segmental pulmonary opacification (eight cases). This was associated with no change in volume, and had poorly defined margins with a tendency for smaller lesions to become confluent. Two patients had extensive opacification (Fig. 1) involving the right lower lobe in one and both lower lobes and the left upper lobe in the other. The other patients showed smaller, irregularly shaped opacities which were only seen in the lower zones and involved less than a quarter of the lung field. These smaller lesions varied in opacity from a very slight loss in translucency to a soft-tissue density (Fig. 2). Complete resolution of these opacities was shown in seven

TABLE II

Radiographic abnormalities

Radiographic abnormality	No. of patients
Extensive confluent opacification	2
Poorly-defined opacities	6
Linear opacities	5
Pleural shadows	4
Cardiomegaly	1

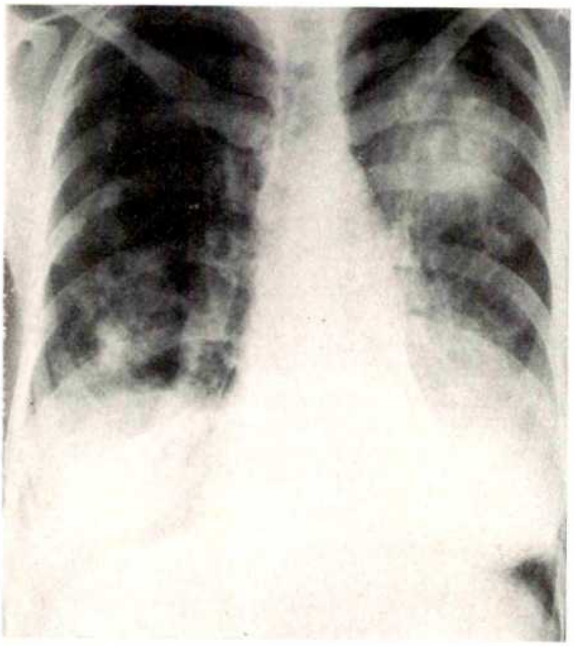


Fig. 1.

Extensive confluent opacification (consolidation) of both lower lobes and left upper lobe. (From Cockshott and Middlemiss, *Clinical Radiology in the Tropics*, 1979)

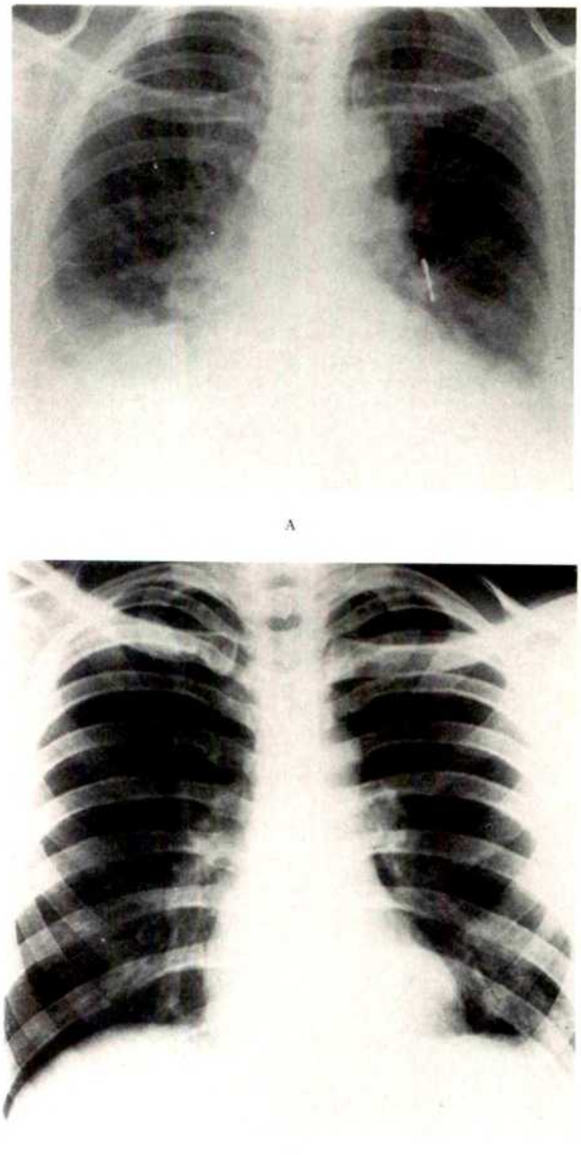


Fig. 2.

(A) Poorly-defined opacification (consolidation) at both bases. Safety-pin artefact in left lower zone.

(B) Poorly-defined opacification (consolidation) in left lower zone. Much softer density opacities than in Fig. 2A.

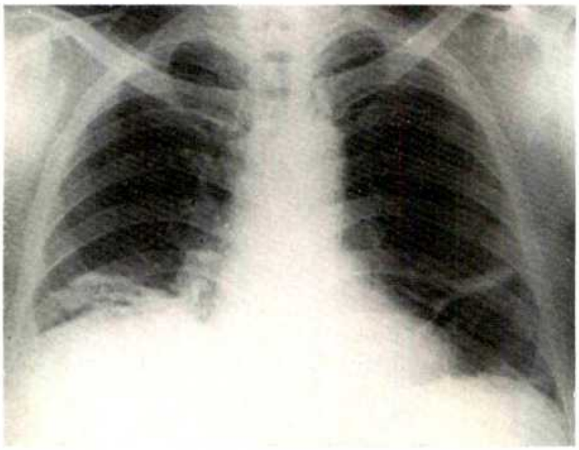
patients within 23 days. In one patient with extensive disease partial resolution was seen at seven days. Two patients at follow-up had basal linear opacities at the site of the previous non-segmental opacities.

Linear opacities extending laterally and upwards from the cardiac borders were seen in five patients (Fig. 3). They were 3–4 mm thick and 7–9 cm long. The upper and lower borders were irregular with short linear extensions into the surrounding lung. Narrower, shorter, linear opacities were seen in the lateral costophrenic recesses of one patient. Only two patients had bilateral disease. Complete resolution was seen in two patients at 14 and 35 days respectively.

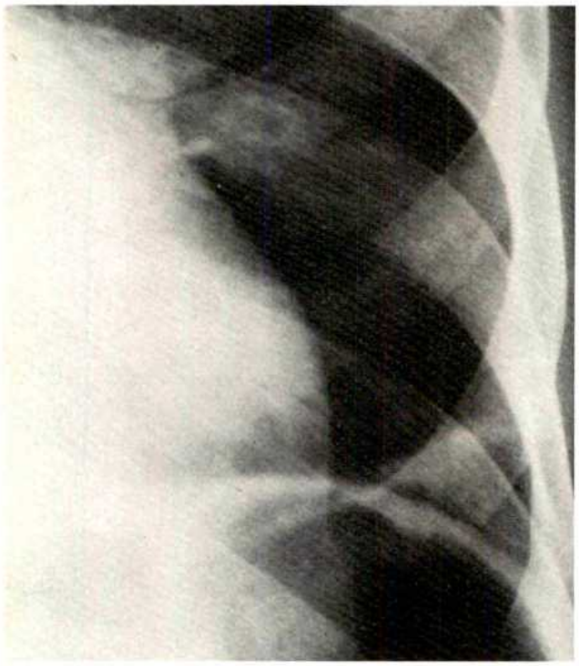
Pleural effusions were seen in four patients (9%). These were bilateral in only one patient. A large effusion was found in one patient (Fig. 4). Small effusions were seen in one patient in association with extensive non-segmental opacification, and one patient had an effusion as his sole radiographic abnormality. Three patients had follow-up films which showed complete resolution in one, partial resolution (at 12 days) in the one with the largest effusion and no change in the other.

Six patients showed no cardiac abnormality. Two had radiological evidence of left ventricular enlargement and two others of biventricular enlargement. Their cardio-thoracic ratios (CTR) were between 0.52 and 0.55. However, an upper limit of normal for the CTR of 0.50 has been shown to be low for Jamaicans of African origin (Ashcroft and Miall, 1969). Using the tables of Ashcroft and Miall (1969) only one of these patients was considered to have cardiomegaly.

No evidence of bony, lymph-node or other soft-tissue abnormality was demonstrated in any patient.



A



B

FIG. 3.

(A) Linear opacities extending laterally from both cardiac borders. These represent areas of subsegmental collapse.

(B) Small area of subsegmental collapse in lateral costophrenic recess.

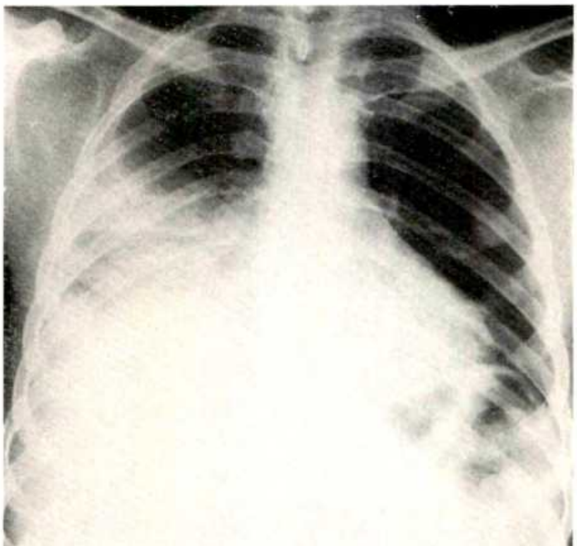


FIG. 4.

Large right pleural effusion shown extending into the horizontal fissure and reaching the lung apex.

TABLE III

CLINICAL FEATURES OF THOSE PATIENTS RADIOGRAPHED

Symptoms/signs	Chest radiograph	
	Abnormal (10)	Normal (34)
Vomiting	6	9
Fever	6	22
Body pains	4	23
Diarrhoea	4	5
Jaundice	4	26
Abnormal chest on examination	4	8
Cough	3	7
Lymphadenopathy	2	6
Headache	1	8

The overall prevalence of abnormal chest films was 23%. Jaundiced patients had a prevalence of chest film abnormality of 13% whereas non-jaundiced patients had a prevalence of 43%. Other symptoms and signs showed no correlation with the presence or absence of chest film abnormality (Table III). Four patients with abnormal films had corresponding signs on clinical examination. Eight of the patients with normal films also had abnormal clinical signs. However, there was no difference in the prevalence of abnormal physical examination of the chest between the two groups.

All patients made complete recoveries. Those with the most extensive radiographic abnormalities took longer to recover from their illness. All had recovered within eight weeks from the onset of illness.

DISCUSSION

The patterns of opacity documented here have been described previously under a variety of titles including "snow-flake-like small patchy lesions" and "confluent massive areas of consolidation" (Wang *et al.*, 1965), "soft, cloudy shadows" and "bronchopneumonic infiltrations" (Ch'iu and Liu, 1959), "localized, patchy cloudings of different sizes" (Research Laboratory of the Sino-Soviet Friendship Hospital, 1959), and "small, patchy, localized infiltrations" and "confluent, larger (even massive) areas of consolidation" (Silverstein, 1953). Miliary opacities have been described in one patient by Petričević and Tomljenović (1980).

The non-segmental opacities are due to consolidation, but rather than representing bacterial pneumonia this is probably a haemorrhagic pneumonitis (Ch'iu and Liu, 1959; Havens *et al.*, 1941; Moeschlin, 1943; Silverstein, 1953; Wang *et al.*, 1965). The predominantly unilateral distribution of these abnormalities makes fluid overload a less likely cause.

The linear opacities were identical to the areas of collapse described by Fleischner (1936) which are commonly seen in patients whose lung bases are poorly ventilated. In one patient there was an ipsilateral diaphragmatic elevation which resolved when the pulmonary lesion disappeared, favouring collapse as the cause. Barrett-Connor *et al.* (1970) describe a patient with "wedge-atelectasis" which may have been a similar lesion.

Three patients with pleural effusions have been described (Barrett-Connor *et al.*, 1970; Feigin *et al.*, 1973; Heath *et al.*, 1965) the largest being estimated to be 300 ml. None of our, or previously described, patients underwent pleurocentesis and thus the nature of the fluid is not known. It is likely that focal haemorrhages, as seen elsewhere in the body, arise in the pleura producing a secondary effusion.

It was felt that the cardiomegaly seen in one patient was not related to leptospirosis as this persisted several months after his leptospirosis had completely resolved. The more usual causes of cardiomegaly in this disorder include fluid overload, myocarditis and pericardial effusion and the heart becomes normal with recovery.

The prevalence of chest film abnormality in this series was less than half that previously reported. Earlier studies have been mainly in China (Ch'iu and Liu, 1959; Research Laboratory of the Sino-Soviet Friendship Hospital, 1959; Wang *et al.*, 1965) and in one was of epidemic victims (Wang *et al.*, 1965). This selection of patients and the natural variation of the disease would account for at least some of the differing results. Our non-jaundiced patients had a prevalence over three times higher than that of the jaundiced ones, contrasting with the findings of the Research Laboratory of the Sino-Soviet Friendship Hospital (1959) in their series of endemic cases. Wang *et al.* (1965) found a high prevalence (67%) in non-jaundiced patients but their study did not include any jaundiced patients. Thus the results published so far confirm that radiographic chest abnormalities are common in both groups and the presence or absence of jaundice is not related to radiological pulmonary involvement.

The most severely ill patients in our series had coughs but these were not a major component of their total clinical picture and did not always correlate with abnormal radiographs. Nery *et al.*, (1977) and Wang *et al.* (1965) also found patients with abnormal chest films and little or no relevant symptomatology, confirming that the clinical picture has no certain predictive value with regard to radiographic abnormality.

Most of our patients gave a history of one to two weeks' illness prior to presentation and no acute onset was recorded. The epidemic patients of Wang *et al.* had acute onsets resulting in early hospital presentation. These patients had abnormal radiographs as early as 24–72 h after onset of illness. They also showed rapid resolution occurring within 3–15 days. Ch'iu and Liu (1959), Poh and Soh (1970) and Silverstein (1953) all describe patients with rapid resolution in a few days. This is in contrast to our findings of a slower rate of resolution which has only been seen before in a "few cases" (Wang *et al.*, 1965). No series has yet reported any long-term abnormalities.

The presence of radiographic pulmonary abnormalities did not allow us to make any predictions about the future clinical course in our patients.

Our results and those of others (Ch'iu and Liu, 1959; Poh and Soh, 1970; Research Laboratory of the Sino-Soviet Friendship Hospital, 1959; Wang *et al.*, 1965), confirm that radiographic pulmonary abnormality is common in in-patients with leptospirosis. These abnormalities are not specific and may mimic other common diseases such as pneumonia, tuberculosis and pulmonary emboli. The abnormalities can be extensive in the absence of physical signs and may be discovered unexpectedly, although those most severely affected usually have respiratory symptoms. No prognostic value can be ascribed to these abnormalities although some patients have died from severe pulmonary involvement. In our experience even extensively affected patients recover completely.

ACKNOWLEDGMENTS

We are indebted to Churchill Livingstone for permission to reproduce Fig. 1, previously published in *Clinical Radiology in the Tropics*, by P. Cockshott and H. Middlemiss, 1979. We would also like to thank Dr. J. Roylance for his constructive criticism.

REFERENCES

ASHCROFT, M. T. and MIALL, W. E., 1969. Cardiothoracic ratios in two Jamaican communities. *American Journal of Epidemiology*, *89*, 161–167.

BARRETT-CONNOR, E., CHILD, C. M. and CARTER, M. J., 1970. Renal failure in leptospirosis. *Southern Medical Journal*, *63*, 580–583.

BURKE, B. J., SEARLE, J. F. and MATTINGLY, D., 1976. Leptospirosis presenting with profuse haemoptysis. *British Medical Journal*, *2*, 982.

CH'IU, Y. C. and LIU, H. H., 1959. Report on observation of roentgenologic pulmonary changes in 48 cases of leptospirosis. *Chinese Journal of Radiology*, *7*, 374–375.

CRUICKSHANK, R., STANDARD, K. L. and RUSSELL, H. B. L., 1976. *Epidemiology and community health in warm climate countries*, (Churchill Livingstone, Edinburgh), p. 185.

FEIGIN, R. D., LOBES, L., ANDERSON, D. and PICKERING, L., 1973. Human leptospirosis from immunised dogs. *Annals of Internal Medicine*, *79*, 777–785.

FLEISCHNER, F., 1936. Über das Wesen der basalen horizontalen Schattenstreifen im Lungenfeld. *Wiener Archiv für innere Medizin*, *28*, 461–480.

HAVENS, W. P., BUCHER, C. J. and REIMANN, H. A., 1941. Leptospirosis: a public health hazard. Report of a small outbreak of Weil's disease in bathers. *Journal of the American Medical Association*, *116*, 289–291.

HEATH, C. W., ALEXANDER, A. D. and GALTON, M. M., 1965. Leptospirosis in the United States. Analysis of 483 cases in man (1949–1961). *New England Journal of Medicine*, *273*, 857–864, 915–922.

MOESCHLIN, S., 1943. Lungeninfiltrate beim Ikterus infectiosus Weil. *Schweizerische Medizinische Wochenschrift*, *73*, 1227–1230.

NERY, L. E., DE PAULA, A. B., NAKATANI, J., DOS SANTOS, M. L. and RATTO, O. R., 1977. Clinical, radiological and functional pulmonary manifestations in patients with leptospirosis. *Revista do Instituto de Medicina Tropical de Sao Paulo*, *19*, 366–373.

PETRIČEVIĆ, I. and TOMLJENOVIĆ, V., 1980. Milijarne plucne promjene u toku leptospiroze—prikaz bolensika. *Liječnički vijesnik*, *102*, 135–136.

POH, S. C. and SOH, C. S., 1970. Lung manifestations in leptospirosis. *Thorax*, *25*, 751–755.

RESEARCH LABORATORY OF THE SINO-SOVIET FRIENDSHIP HOSPITAL and PEKING PEOPLE'S HOSPITAL, 1959. Pathophysiological studies on leptospirosis. IV. Roentgenological manifestations of chest films. *Chinese Journal of Internal Medicine*, *7*, 971–978.

SILVERSTEIN, C. M., 1953. Pulmonary manifestations of leptospirosis. *Radiology*, *61*, 327–334.

SPINK, W. W., 1978. *Infectious Diseases. Prevention and Treatment in the Nineteenth and Twentieth Centuries*, (Wm. Dawson & Son Ltd., London), p. 249.

WANG, C. P., CH'I, C. W. and LU, F. L., 1965. Studies on anicteric leptospirosis. III. Roentgenologic observation of pulmonary changes. *Chinese Medical Journal*, *84*, 298–306.

1981, *British Journal of Radiology*, 54, 944–947

An assessment of intravenous urogram imaging using 100 mm and conventional films

By *Elizabeth M. Robertson, M.B., Ch.B., D.M.R.D., †B. Baily, M.Sc., †Tamarisk M. Hearnden, M.Sc., †R. F. Mould, Ph.D., F.Inst.P., F.I.S. and *D. H. Trapnell, M.D., F.R.C.P., F.R.C.R.

*Department of Diagnostic Radiology, Queen Mary's Hospital, London SW15 and †Department of Medical Physics, Westminster Hospital, London SW1

(Received March 1981 and in revised form May 1981)

ABSTRACT

A clinical trial was designed to compare the amount of useful diagnostic information obtained from the ten-minute (24×30 cm) film of an IVU when using either indirect (100 mm) or conventional radiography. The films for 50 patients were independently examined by ten radiologists. Eight observers considered conventional radiography to be significantly better than indirect (100 mm) radiography, $P < 0.05$, and two observers considered that there was no significant difference. Possible applications of indirect radiography are briefly described.

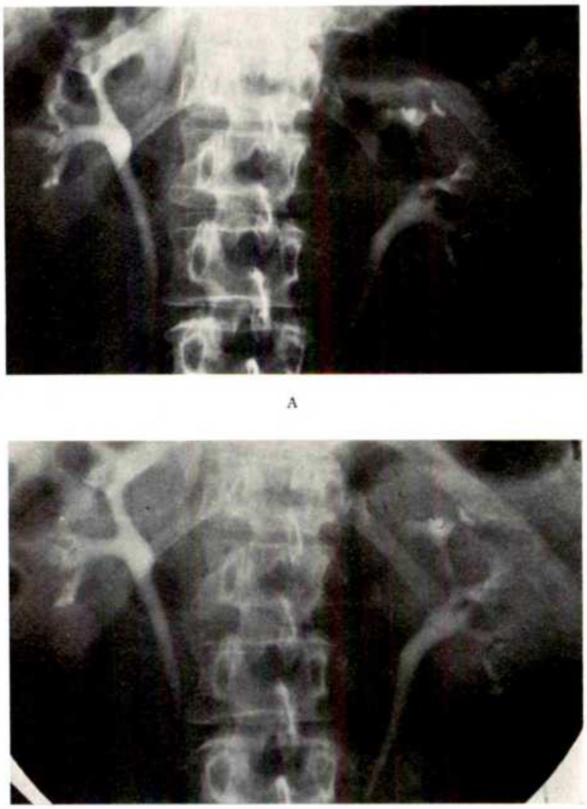
Two coincident developments in the design of radiographic equipment have made possible a method of recording the radiographic image which produces a significant reduction of dose and costs of materials—(i) the production of high-resolution tubes and (ii) the availability of 100 mm cameras. In the United Kingdom to date there has not been any trial of 100 mm indirect radiography of an examination such as the intravenous urogram (IVU), whereas this technique has been extensively used for recording fluoroscopic procedures.

MATERIALS AND METHODS

In order to obtain a valid comparison of the large and small films (Fig. 1), an additional radiograph had to be taken. For this reason all the patients were over 40 years of age and the majority were over 60 years. The additional radiation dose received from the 100 mm indirect radiographic investigation depends upon the radiographic exposure, which is related to the size of the patient. We found by thermoluminescence dosimetry that the skin dose did not exceed 7 mGy (700 mrad).

Equipment

The small films were made utilizing (i) a caesium iodide high-resolution intensifier placed beneath a Koordinate Kombi radiography table, (ii) a standard Siemens Sircam 100/2 film camera, and (iii) a ceiling-suspended Biangulix X-ray tube with 0.6 mm/1.2 mm focal spot. The intensifier was mounted on fixed floor tracks so that it could be accurately positioned in precisely the location of the standard pedestal Bucky, which was also modified to run on the same floor tracks. Thus, the centering of the large and small films was identical. A copy of each ten-minute standard (24×30 cm) film was made and kept with the patient's IVU series. The original large film and the 100 mm film were retained for the trial. For the large film, the standard radiographic technique currently in use in the department was employed. No special procedures were adopted. For larger patients, the 24×30 cm films were made with



A

B

FIG. 1.

Examples of intravenous urograms on large film (A) and small film (B).

Based on a talk at a BIR meeting, "Radiographic systems—what is best?", held on March 18, 1981.

rare-earth screens, while standard screens were used with the remainder.

The same kV, tube–film distance, field size and centering were used for both 100 mm and large films. The mAs for the small film was automatically regulated by a phototimer at the intensifier output phosphor. The ten-minute IVU film was selected for the comparison of techniques so that the 100 mm radiograph in no way interfered with the routine examination. The standard film was always made first. By using the same field size for the small film we exposed slightly more of the patient than was strictly necessary, but we considered this desirable so that the absorbed dose for the two techniques could be compared. If we had used a 23 cm diameter field a further slight reduction in dose might have been possible. Finally, some measurements were made by thermoluminescence dosimetry to confirm that the dose received by the patient is reduced when 100 mm indirect radiography is used, as suggested by the literature (Berridge and Haybittle, 1975; Rautenburg, 1975; Schuster and Heinrich, 1974; Wohl and Koehler, 1965).

Design of trial

The films were read by ten different radiologists to whom the films were presented in random order so that the readers could not make a direct comparison between a large film and a small film for an individual patient. The trial was therefore organized to eliminate the possibility of bias on the part of a reader. The small films were assessed using a magnifying lens. The trial co-ordinator (E.M.R.), although a radiologist, did not act as a film reader. Five features were used for assessment in each of the 100 films, and these are shown schematically in Fig. 2. Each feature was assessed as either visible or invisible and correspondingly scored either as one or zero. The maximum possible total score accorded to any film by an individual reader was therefore five, and the minimum possible total score per film was

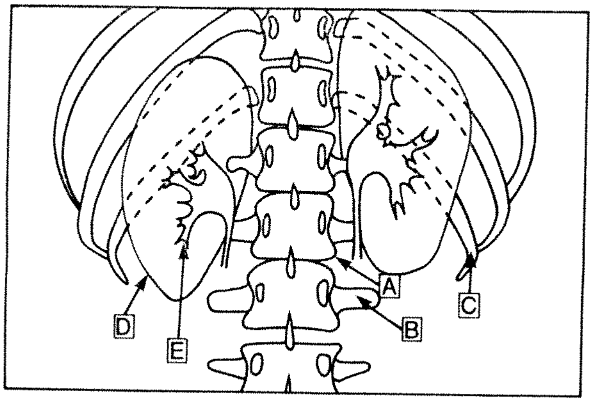


FIG. 2.

The five features used to assess the resolution of intravenous urogram images. A, trabecular pattern of vertebral bodies; B, definition of transverse process of L3. C, definition of 12th ribs; D, definition of right renal outline; E, definition of calyces.

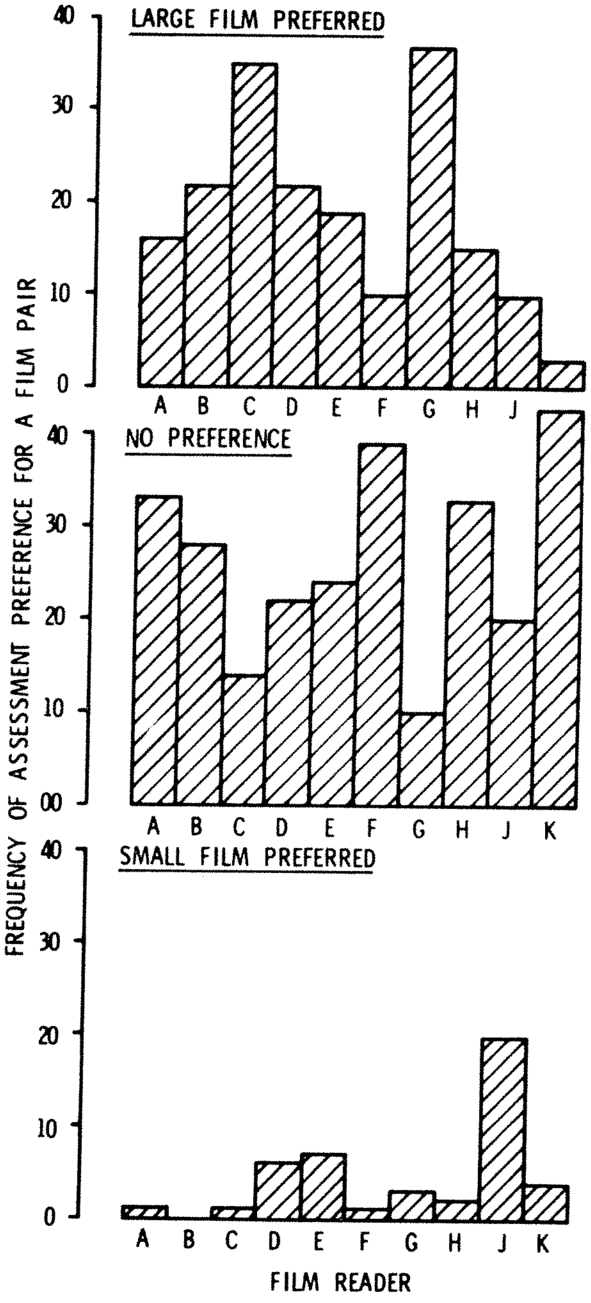


FIG. 3.

Diagram showing reader performance for 50 film pairs and ten readers in terms of individual preferences for each reader.

zero. The results were analysed using the Wilcoxon matched pairs signed ranks test (Siegel, 1956) for each of the ten readers.

RESULTS

The performance of the ten readers for the 50 pairs of films is shown in Fig. 3 where the histogram blocks show the preference frequency of the individual readers A–K. This diagram represents a total of 500 assessments of pairs of films and indicates that in 37.8% (189/500) there was a preference for the large film, in 9.0% (45/500) there was a preference for the small film, and in 53.2% (266/500) there were tied scores for the large and small films.

When the Wilcoxon test was applied to the data summarized in Fig. 3, it was found that two readers (J and K) considered that there was no significant difference between large and small films, $P > 0.05$; seven readers considered the difference to be significant in favour of the large film, $P < 0.01$; and one reader (F) considered the difference to be significant in favour of the large film, $0.02 < P < 0.01$.

There were 2500 individual feature assessments for each type of film (50 films × 10 readers per film × five assessment features per film). Of these, 10.1% (253/2500) were scored as invisible in the large films and 17.7% (443/2500) were scored as invisible in the small films. The distribution of these zero scores among the different assessment features is given in Table I.

TABLE I

DISTRIBUTION OF ZERO SCORES FOR LARGE AND SMALL FILMS

Assessment feature (notation in Fig. 2 given in brackets	Number of zero scores (feature assessed as invisible)	
	Small film	Large film
Trabecular pattern of vertebral bodies (A)	134	54
Definition of right renal outline (D)	106	60
Definition of transverse process of L3 (B)	77	48
Definition of calyces (E)	71	62
Definition of 12th ribs (C)	55	29
Total number of zero scores	443	253

DISCUSSION

The trial was undertaken because there are three reasons why it is highly desirable to undertake standard radiographic procedures using small films. These are (i) the reduction in dose to the patient, (ii) the reduction in the cost of the film and chemicals, and (iii) the conservation of silver stocks. Thermoluminescence dosimetry confirmed the results of previous reported work in that, dependent upon radiographic exposure, the dose reduction factor achieved using small films is in the range two to six for rare-earth screens and six to 12 for standard screens. The cost reduction factor for film is of the order of five. Since it appears that the world stocks of silver are likely to be exhausted within some 30 years, conservation must be taken seriously. However, from the results presented it has not been demonstrated that for intravenous urography the use of 100 mm indirect radiographs provides, in terms of image resolution, an acceptable alternative to conventional large film radiographs.

For the small film the trabecular pattern of the vertebral bodies was the least distinguishable feature (Table I). Only in the case of the definition of the calyces was the difficulty in assessing the large film similar to the difficulty encountered with the small film.

The smaller circular format of the image in the 100 mm film resulting from the 23 cm diameter of the intensifier imposes a distinct limitation on the value of the small film in intravenous urography. In this series, one or other kidney was normally incompletely shown in the 100 mm film. Thus, if this indirect radiographic technique were to be used exclusively with a 23 cm intensifier, there would have to be a significant modification of the standard IVU techniques used in most departments. The use of a 33.5 cm intensifier might overcome some of these problems but we suspect that unless the resolution of the intensifier can be greatly improved, small abnormalities such as nephrocalcinosis could be overlooked if 100 mm films are used alone.

CONCLUSIONS

Whilst indirect 100 mm radiography does not provide a suitable alternative to conventional radiography for all intravenous urography, we believe that the technique may have a useful role in certain special circumstances. These might include monitoring renal function following removal of an obstruction, checking the position of a kidney before renal biopsy, and confirming the position of a drainage tube or catheter. There may also be a place for the technique at least as a part-replacement of standard films when examining children, since the small size of the intensifier will not be such a disadvantage in these circumstances.

ACKNOWLEDGMENTS

We are indebted to all the radiographers at Queen Mary's Hospital who so kindly co-operated in this trial, particularly Miss Susan Scott, Superintendent Radiographer. We would like to acknowledge the help provided by the following radiologists who acted as film readers: Drs. L. Davison, A. Dux, K. Franklin, R. Kendrick, L. Moss, E. O'Sullivan, K. Riahy, H. Shojai and K. Thomas. We would like to thank Mr. Laurence Freedman for helpful discussions on statistical aspects. Also, we are grateful to the Department of Health and Social Security, particularly Mr. Colin Hancock and Mr. Gordon Higson, for providing the 100 mm camera which made this trial possible, and to the Westminster Hospital Research Committee for a grant to make this study possible. Finally, we would like to thank Miss Christine Bundle for secretarial assistance.

REFERENCES

BERRIDGE, F. R. and HAYBITTLE, J., 1975. Some aspects of 70 and 100 mm radiography during fluoroscopic procedures. *British Journal of Radiology, 48*, 943.

RAUTENBURG, H. W., 1975. Cinefluorography, serial radiography with the image intensifier and the large-format film changer for paediatric angiocardiography. *Electromedica, 5/75*, 179–184.

SCHUSTER, W. and HEINRICH, H., 1974. Dose requirements in direct and indirect radiography with high resolution X-ray image intensifier tubes. *Annales de Radiologie, 17*, 427–433.

SIEGEL, S., 1956. *Non parametric statistics for the behavioural sciences* (McGraw-Hill, New York), pp. 75–83.

WOHL, G. T. and KOEHLER, P. R., 1965. Experience with a 70 mm camera in image amplification fluorography. *Clinical Radiology, 16*, 363–368.

Book review

Multiple Imaging Procedures. 4. Urinary Tract and Adrenal Glands. Imaging and Diagnosis. By Ernest J. Ferris and Joanna J. Seibert, pp. ix+535 illus., 1980 (Grune and Stratton, New York), $59.50.
ISBN 0-8089-1296-8

Following a sustained period of relative famine, there is now a veritable glut of textbooks of radiology of the urinary tract, some including the genital tract and others the suprarenals. This harvest of books has paralleled the proliferation of both the number and application of new techniques for the diagnosis, evaluation and treatment of urinary-tract disease. New textbooks of uroradiology must therefore be assessed in general on their overall contribution to the literature and in particular on the success achieved in incorporating discussion of the relative merits of the numerous imaging techniques currently available.

This well-presented volume, the fourth of a new series produced under the overall title of *Multiple Imaging Procedures*, is edited by Ernest J. Ferris and Joanna J. Seibert with four additional authors. The first section comprises five chapters devoted to the methods of performing urography, ultrasound, nuclear medicine, computed tomography and renal angiography with detailed accounts of the normal findings in each technique. The first chapter also includes an excellent succinct review of current views on embryology of the urinary tract. The second section is the major portion of the book and comprises some 12 chapters, each dealing with a group of renal disorders. Each chapter opens with a description of the basic pathology and an outline of the presenting clinical features of the diseases under discussion. The group of diseases is then discussed under the headings of conventional urography, ultrasound, nuclear medicine, CT and angiography. This format allows the findings and role of each investigation to be discussed in detail for each group of diseases, but does make it tiresome to attempt to discover the appearances of any single disease entity. The newer imaging techniques are reviewed in depth, accurately reflecting current thinking. In common with most accounts of the new techniques, there is a tendency to denigrate the role of conventional studies and the reader will have to seek elsewhere for adequate accounts of the appearances to be found by excretion urography. The third section comprises one chapter devoted to the suprarenals and follows the style of the preceding section.

The profuse illustrations are well selected with the exception of many of the ultrasound images which do not reflect the improved definition available from modern equipment. There is a satisfactory index. Relatively few references are appended to each chapter and those that appear have been selected predominantly from the American literature.

In all, this is an excellent review of the relative merits of the newer techniques presented in a rational manner. It will prove invaluable to the experienced radiologist, but the trainee will undoubtedly need to study other accounts of conventional methods to achieve benefit from this volume. It can be warmly recommended for inclusion in libraries of both working departments and teaching units, but, if it is to remain up to date and of maximum value, it will require the production of frequent new editions to reflect advances in a still rapidly developing field.

J. ROYLANCE.

1981, *British Journal of Radiology*, 54, 948–952

Initial findings in the computer-aided diagnosis of cerebral tumours using CT scan results

By *K. Wills, B.Sc., †G. H. du Boulay, M.B., B.S., F.R.C.P., F.R.C.R. and *D. Teather, M.Sc.

*School of Mathematics, Computing and Statistics, Leicester Polytechnic, Leicester and
†Lysholm Radiological Department, The National Hospital for Nervous Diseases, Queen Square,
London WC1N 3BG

(*Received August 1980 and in revised form July 1981*)

ABSTRACT

This paper describes the initial findings of computer-assisted diagnosis of cerebral tumours using Bayes' Theorem and CT scans. For various sets of signs, tables of accuracy and reliability have been constructed, and a computer *versus* radiologist analysis for three types of tumour has been made. Based only on the results of CT scans, the computer has produced diagnoses relatively quickly, and overall these are of reasonable accuracy when compared with the radiologists' reports. The worst results occurred in the prediction of meningiomas, the reasons for which will be examined in subsequent work.

This paper considers the statistical methodology and initial findings of a system for computer-aided diagnosis of cerebral tumours using a microprocessor and employing Bayes' Theorem.

Independence

A computer-assisted approach to diagnosis based on the use of Bayes' Theorem has been thoroughly tested in the case of diagnosis of jaundice (Knill-Jones *et al.*, 1973) and the acute abdomen (de Dombal *et al.*, 1972). The problem with the method, when using Bayes' Theorem, is that there are so many sign profiles for each disease; for example, with five signs there are 32 profiles per disease and with ten signs there are 1024 profiles per disease.

To overcome such problems it is common practice to assume that the signs are independent within each disease category (Taylor, 1970; Teather, 1974a); that is, the occurrence of a particular sign does not depend upon the presence or absence of any other sign. If that is so, all we need to know is the incidence of positive results in each disease for each separate sign. The probability of a particular profile is then obtained by simply multiplying the appropriate individual incidences. Computation is easily performed on a small microprocessor.

The prior incidences of the disease $p(D_i)$ and the probability of test results within each disease $p(S_j/D_i)$ must be estimated from a data base of past patients' records, for which both test results and confirmed diagnoses must be available.

In practice, once a substantial data base has been collected, it is possible to identify many, perhaps most, of the dependencies and to eliminate them. One of the aims of this study is to determine the success of computer-assisted diagnosis after the elimination of obviously dependent signs.

Computer hardware

The equipment (described in Table I) on which the system is being developed was chosen for its reliability (we have had no system failure), ready availability and operational speed.

Computer software

The software, written in BASIC and with minor modifications transferable to other computers, is designed to cope with the required number of disease categories and tests for each disease category.

METHOD

By defining a series of signs which describe the

TABLE I

SYSTEM COSTS AND DESCRIPTIONS

Device	Characteristics	Approximate cost at time of purchase £
Commodore PET Computer	32 Kbytes with VDU and keyboard	800
Dual floppy disk drives	340 Kbytes of store	800
Printer	300 Chrs/sec	800
Cables/disks/etc.		100
		2500

CT image and 114 disease categories derived from a somewhat larger list (du Boulay and Price, 1968), a data base of past patients with confirmed diagnoses is being established. The signs are listed in Table II. The information about position has in practice been simplified by grouping the 44 possible signs under only nine headings and using these for the computation.

The current size of the data base is 383 cases of known diagnoses (Table III). All the tumours have been proven by histological examination. The diagnoses of the non-tumours have been established by clinical examination and observation of progress over a number of years. From these patients' records it has been possible to estimate the prior probability for each disease (*e.g.* the incidence of gliomas in the data

TABLE II

SIGNS ON CT

Number of lesions

- Single lesion
- Multiple lesions

Position

- Parasagittal
  - Frontal
  - Parietal
  - Occipital
- Superficial only other than parasagittal
  - Frontal
  - Temporal
  - Parietal
  - Occipital
- Deeply placed
  - Diencephalon
  - Frontal
  - Temporal
  - Parietal
  - Occipital
- Both deeply placed and superficial
  - Frontal
  - Temporal
  - Parietal
  - Occipital
- Subfrontal
  - Mid-line
  - Lateral
- Central
  - In or above 3rd ventricle
  - In or below 3rd ventricle
- Intraventricular
  - Lateral ventricle
  - 4th ventricle
- Parasellar
- Intrasellar
- Intraosseous—vault
- Intrasseous—skull base
  - Anterior fossa
  - Middle fossa (±sphenoid ridge, ±anterior clinoids)
  - Petrous apex
  - Internal auditory meatus
- Jugular foramen
- Other posterior fossa
- Cisternal
  - Chiasmatic or interpeduncular
  - Pontine
  - Cerebello-pontine angle
  - Quadrigeminal
  - Ambient
  - Cisterna magna
- Posterior fossa
  - Mid-line anterior
  - Mid-line posterior
  - Antero-lateral
  - Postero-lateral
  - Lateral
- High brainstem
- Cortical sulci over cortex

Unenhanced appearance (attenuation values)

- Homogeneous
- Heterogeneous
- Probably calcified
- Lower than bone, higher than brain
- Isodense with brain
- Lower than brain higher than CSF
- Equal to CSF
- Homogeneous with concentric low surround
- Homogeneous with concentric high surround
- Lentiform or mantle shape

Enhancement

- Homogeneous
  - Of entire lesion
  - With surrounding unenhanced abnormal area
- Ring
  - With lower than brain-attenuation centre
  - With isodense or higher than brain-attenuation centre
  - Multiple rings
  - Thickness of ring is uniform within 25%
- Of apparently abnormal blood vessels
- Selectively of grey matter
- Heterogeneous other than above
- Did not enhance

Other signs and qualifiers

- Mass effect
- Expansion of—
- Compression of—
- Dilatation of both lateral ventricles
- Dilatation of 3rd and both lateral ventricles

base) and the probability of a certain sign in each disease (*e.g.* the incidence of mass effect amongst gliomas).

In the original list there were 114 disease categories, taking into consideration the fact that the same tumour type was sometimes counted more than once because it could occur in several situations. Some of the categories are not represented in the data base as yet; therefore, initially, the work has been carried out to determine tumour type diagnosis alone. This reduced the diagnostic problem to differentiation between 24 possible diseases (Table III).

TABLE III

THE MATERIAL

Disease categories	Cases in data base	Cases tested
1 Meningioma	24	12
2 Glioma, type unspecified	40	20
3 Glioma, astrocytoma grade IV	14	7
4 Chromophobe adenoma	8	4
5 Metastasis	18	9
6 Eosinophil adenoma	2	1
7 Craniopharyngioma	5	2
8 Chordoma	1	1
9 Epidermoid	1	0
10 Haemangio and haemangioblastoma	2	1
11 Abscess	2	1
12 Haematoma, intracerebral	38	19
13 Haematoma, subdural	13	7
14 Haematoma, extradural	1	0
15 Non-neoplastic cyst	0	0
16 Arachnoid cyst	0	0
17 Colloid cyst	0	0
18 Choroid plexus papilloma	1	1
19 Neurinoma, 5th nerve	0	0
20 Neurinoma, 7th nerve	0	.0
21 Neurinoma, 8th nerve	5	2
22 Glomus jugulare tumour	0	0
23 Pinealoma	1	1
	176	88
24 Not tumour (classified together as non-tumour)	207	103
Total	383	191

It was decided to apply Bayes' Theorem and, for three main reasons, to introduce one set of symptoms at a time:

(a) to see if Bayes' Theorem were a suitable method to apply;

(b) to see how the progressive introduction of sets of signs affected diagnosis;

(c) to provide a simple basic method which could be improved by later elaboration.

For instance, there are indications that some signs may not be independent whilst others may be redundant. This will be taken into account in future analysis.

Application of Bayes' Theorem using cross-validation

To assess the accuracy of the computer's predictions, the cross-validation technique was applied (Lachenbruch and Mickey, 1968). Using this technique, a single case was removed from the data base and the remainder used to estimate the required probabilities. Bayes' Theorem was then used by the computer to predict the disease of the extracted case; in this way it was possible to compare computer prediction with actual pathology. This technique was repeated for each alternate case (Table III).

Separate sample validation

In order to assess the cross-validation technique, a completely new data base of 50 cases was tested. Prior and conditional probabilities were calculated on the previous data base of 383 cases and the 50 new cases were then analysed. The results confirmed the accuracy of the technique.

RESULTS

Tables IV, V and VI give summaries of the results. They show the "accuracy" and "reliability"

TABLE IV

SEPARATING "TUMOURS" FROM "NON-TUMOURS"

	Accuracy		Reliability	
	Tumour	Non-tumour	Tumour	Non-tumour
Position alone	13.6% (3.7%)	99.0% (0.97%)	92.3% (7.4%)	57.3% (3.7%)
Position + unenhanced appearance	88.6% (3.4%)	81.6% (3.8%)	80.4% (4.0%)	89.4% (3.2%)
Position + unenhanced and enhanced appearance	85.2% (3.8%)	82.5% (3.7%)	80.6% (4.1%)	86.7% (3.4%)
Position + unenhanced and enhanced appearances, together with other signs	90.9% (3.1%)	85.4% (3.5%)	84.2% (3.7%)	91.7% (2.8%)
All possible signs	89.8% (3.2%)	87.4% (3.3%)	85.9% (3.6%)	90.9% (2.9%)

Figures in parentheses are standard errors. Approximate 95% confidence limits are given by ±2 standard errors with an upper cut off at 100%.

TABLE V

PERCENTAGE ACCURACY IN DIAGNOSING TUMOUR TYPE

Diagnosis made from	Tumours				Non-tumours				Overall			
	1st	2nd	3rd	Total	1st	2nd	3rd	Total	1st	2nd	3rd	Total
Position alone	2%	15%	35%	52% (5.3%)	99%	0%	0%	99% (0.97%)	54%	7%	16%	77% (3.0%)
Position + unenhanced appearance	44%	13%	6%	63% (5.2%)	82%	5%	7%	93% (2.5%)	64%	8%	6%	79% (2.9%)
Position + unenhanced and enhanced appearances	47%	18%	11%	76% (4.5%)	83%	9%	1%	92% (2.6%)	66%	13%	6%	85% (2.6%)
Position + unenhanced and enhanced appearances, together with other signs	45%	20%	11%	77% (4.5%)	85%	6%	4%	95% (2.1%)	67%	13%	7%	87% (2.4%)
All possible signs	47%	19%	11%	77% (4.5%)	87%	4%	7%	98% (1.4%)	69%	11%	9%	88% (2.4%)

Figures in parenthesis are standard errors. Approximate 95% confidence limits are given by ±2 standard errors with an upper cut-off at 100%.

of the method in discriminating between tumours and diseases other than tumours (these have been grouped together as non-tumours).

"Accuracy" and "reliability" are the measures of success commonly employed in work on computer-assisted diagnosis (Burbank, 1969; de Dombal *et al.*, 1972; Knill-Jones *et al.*, 1973; Teather, 1974b; Horrocks, 1974). In our work, accuracy means how often a disease is correctly diagnosed as first choice (*i.e.* the number of correct diagnoses/number of cases of the disease in the test sample); reliability means how often the prediction of a particular disease proves correct (*i.e.* the number of correct diagnoses/the number of times the disease is diagnosed). Radiologists are more used to the terms "sensitivity" and "selectivity" as definitions of the value of a diagnostic test. "Accuracy" has much in common with "sensitivity", and "reliability" is like "selectivity".

Table IV shows the discrimination between tumour and non-tumour, without taking into account the nature of the lesion. Bayes' Theorem was also used to predict the exact tumour type.

Table V shows the accuracy of Bayes' Theorem in more precisely predicting the nature of lesions stage by stage. For example, working from position alone, Bayes' Theorem correctly identified the nature of 2% of tumours as first choice, 15% as second choice and 35% as third choice; an accuracy of 52% for the first three places. When the un-enhanced appearance (*i.e.* the plain scan sign description) was added to the data, 44% of tumours were correctly identified as first choice, 13% as second choice and 6% as third choice; an accuracy of 63% for the first three places. The further addition of the enhanced appearance (*i.e.* after injection of an organic iodine compound) slightly improved tumour accuracy.

Comparison of accuracy

Using Bayes' Theorem on the CT scan results, a comparison was made between the computer's predictions and the radiological reports. The reports on these 6500 to 8000 patients were produced, after careful consideration, at daily conferences in the X-ray Department of the National Hospital, Queen Square, under the chairmanship of several different consultant radiologists (including the second author in about one-third of the cases). The reports were made with a knowledge, at least, of the information given on the request form, often with a knowledge of further clinical data, and the results of other radiological investigations. Each report was first written by a trainee radiologist and then dicussed subsequently by the other radiologists present; the final

TABLE VI

COMPARISON OF ACCURACY BETWEEN THE COMPUTER METHOD AND A GROUP OF RADIOLOGISTS

	Glioma		Meningioma		Metastasis	
	Computer	Radiologists	Computer	Radiologists	Computer	Radiologists
Total CT materials	191	6500	191	8000	191	6500
Proved pathology	27	179	12	100	9	29
No. correctly diagnosed as 1st choice	20	119	6	90	3	9
No. incorrectly diagnosed	12	35	7	20	8	41
Accuracy	74% (54–84)	66% (59–73)	50% (21–79)	90% (82–93)	33% (75–70)	31% (16–54)
Reliability	63% (44–79)	77% (70–84)	46% (19–75)	82% (73–88)	27% (60–61)	18% (86–31)

report represented a committee decision. These reports were later analysed by Claveria *et al.* (1978), and they form the basis for our comparison of radiologists' diagnostic success in cases of glioma and metastasis. The radiologists' diagnostic success in cases of meningioma were discussed by Sutton and Claveria (1977). The cases in this present study of computer-assisted diagnosis came from this much larger material.

The descriptions of all the CT scans, on which the present computer-assisted diagnoses are based, were made several years later without the radiologist (second author) knowing the final diagnoses. In more than half the cases the original reports were written by other radiologists; the remainder were written in combination with the second author.

Table VI is a comparison of success with three types of tumour: glioma, meningioma and metastasis. There was no significant difference between the radiologists' and the computers' predictions for gliomas and metastasis, but the computers' prediction of the diagnosis in meningioma cases and of meningiomas were less accurate and less reliable.

The meningioma problem

The poor diagnostic performance with the meningioma cases needs an explanation. It did not appear to be due entirely to the radiologists' knowledge of either the plain X-ray findings or the patients' history. Examination of the data revealed that all the computer's false negatives were similar in one respect: the meningiomas arose from either the sphenoid ridge or the sellar region; in addition, many of them were not accompanied by the low attenuation of oedema. This knowledge opened the way to an improvement in the computer program and will be discussed in a later paper.

REFERENCES

BURBANK, F., 1969. A computer diagnostic system for the diagnosis of prolonged undifferentiating liver disease. *American Journal of Medicine*, *46*, 401–414.

CLAVERIA, L. E., DU BOULAY, G. H. and KENDALL, B. E., 1978. The diagnostic limitations of computerized axial tomography in hemispheric tumours. In *The Diagnostic Limitations of Computerized Axial Tomography*, ed. J. Bories (Springer-Verlag, Berlin/Heidelberg/New York), pp. 2–16.

DE DOMBAL, F. T., LEAPER, D. J., STANILAND, J. R., McCAN, A. P. and HORROCKS, J., 1972. Computer aided-diagnosis of acute abdominal pains. *British Medical Journal*, *ii*, 9–13.

DU BOULAY, G. H. and PRICE, V. E., 1968. The diagnosis of intracranial tumours assisted by computer. *British Journal of Radiology*, *41*, 762–781.

HORROCKS, J. C., 1974. A computer-aided diagnostic system using a small desk-top computer calculator. *Methods of Information in Medicine*, *13*, 83–88.

KNILL-JONES, R. P., STERN, R. B., GRIMES, D. H., MAXWELL, J. D., THOMPSON, R. P. H. and WILLIAMS, R., 1973. The use of a sequential Bayesian model in the diagnosis of jaundice by computer. *British Medical Journal*, *i*, 530–533.

LACHENBRUCH, P. A. and MICKEY, M. R., 1968. Estimation of error rates in discriminate analysis. *Technometrics*, *10*, 1.

SUTTON, D. and CLAVERIA, L. E., 1977. Meningiomas diagnosed by scanning: a review of 100 intracranial cases. In *First European Seminar on Computerised Axial Tomography in Clinical Practice*, eds. G. H. du Boulay and I. F. Moseley (Springer-Verlag, Berlin/Heidelberg/New York), pp. 102–108.

TAYLOR, T. R., 1970. Computer-guided diagnosis. *Journal of the Royal College of Physicians*, *4*, 188–195.

TEATHER, D., 1974a. Diagnosis—method and analysis. *Bulletin of the Institute of Mathematics*, *10*, 37–41.

1974b. Statistical techniques for diagnosis. *Journal of the Royal Statistical Society, Series A*, *137*, 231–244.

1981, *British Journal of Radiology*, 54, 953–954 NOVEMBER 1981

CT brain scans: part of a 20-year development study following gross undernutrition during infancy

By L. C. Handler, M. B. Stoch and P. M. Smythe

Departments of Neuroradiology, Psychiatry and Paediatrics, Groote Schuur Hospital and University of Cape Town

(*Received February 1981*)

ABSTRACT

CT brain scans on 20 individuals aged 20–24, who were grossly undernourished during infancy, and on 20 controls, showed no significant differences either between the groups or within individuals. On highly critical evaluation, five previously undernourished individuals had minimal changes not considered significant on routine CT scanning which correlated positively with tests for disturbances of visuomotor organization.

Always there was concern that some of the infants who were selected from 1955–59 to try to ascertain whether the age at which undernutrition occurs is critical for subsequent brain growth and intellectual development, might have had organic brain damage. Furthermore, it has been suggested that undernutrition during infancy may cause brain atrophy (Monckeberg, 1975). To clarify these questions and to find out whether any anatomical changes occur in the adult brain as a result of undernutrition during infancy, CT scans have been carried out on the 40 subjects previously reported (Stoch and Smythe, 1963; 1967; 1976).

METHOD

The 20 individuals who were marasmic during infancy and formed the index group, as well as the 20 controls, volunteered for CT scanning. An EMI scanner (180 × 180 matrix waterbag model), was used to make three standard cuts without contrast enhancement, as this was considered not ethically justifiable.

RESULTS

Routine crude evaluation of the scans for the absorption coefficient of cerebral tissue showed that with one exception there was no significant difference between groups nor within various regions of individual cerebral tissue. The one exception had a slight increase in density (19–20, cerebral tissue 17) of both caudate nuclei, which reflects either an increase in grey matter density or very early basal ganglia calcification. This is a recognized normal finding unassociated with any neurological deficit. The coronal distance across the anterior horns was measured and the cella media evaluated as an index of ventricular size. No significant abnormality nor differences in size were noted within individuals or within groups. No significant evidence of cortical atrophy was observed.

Highly critical evaluation, however, elicited the following minor changes in three girls and two boys of the index group: mild cortical atrophy in the region of both temporo-parietal regions L > R (Fig. 1); a small focus of cortical atrophy on the medial aspect of the right parietal lobe; a minute focus of right insular atrophy; a minute interhemispheral focus high up in the fronto-parietal region; a small focus of atrophy in the region of the right insula with an overlying single dilated sulcus (this could have been due to head injury, as the child had a recent history of fits). Amongst the control group, only a calcific fleck above the dorsum sellae and increased density of the heads of the caudate nuclei were seen in one subject. In terms of routine clinical

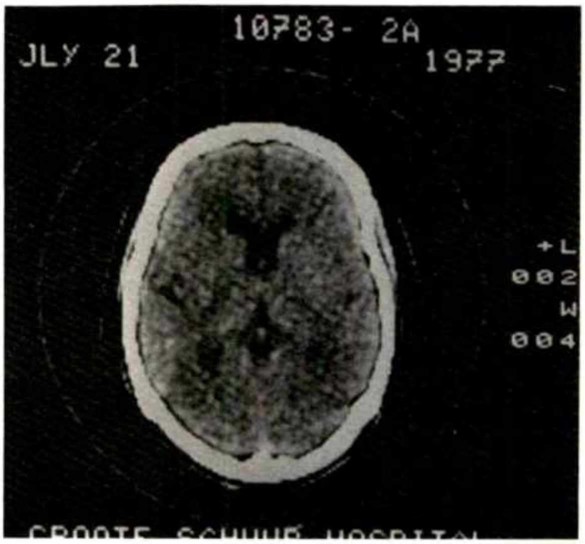


FIG. 1.

CT scan of index girl aged 21 years showing mild cortical atrophy in both temporo-parietal regions, more marked on the left. Lateral ventricles are not dilated.

CT scanning for epilepsy none of these changes would be considered significant.

Earlier cognitive and anthropometric data of the index subjects who showed minimal atrophy on CT scan were compared with the data of index subjects with no CT changes by taking the proportion of each group who scored below the median for the whole index group. Significantly worse scores at $p=0.1$ level were found in the individuals with minimal CT changes in the Bender Visual Motor Gestalt Test, Human Figure Drawing and Pattern Completion sub-test of the New South African Individual Scale carried out in 1973. No correlation was found with the one control subject. No correlation was found between the CT scans and the electroencephalograms done in 1973.

Discussion

Initially, and when judged on routine standards, it seemed that no significant differences or abnormalities could be detected on CT scans of adults who had been grossly undernourished during the first two years of life. This would be in keeping with the concept that although undernutrition in infancy may result in a brain smaller than optimal as judged by head circumference (Stoch and Smythe, 1976), by brain weight (Brown, 1965), and deficient in neuronal development (Winick and Rosso, 1969), only growth retardation occurs and not atrophy. But when the five individuals who showed minimal changes on highly critical evaluation were compared for their intellectual performances with the remaining 15 of the index group quite a marked correlation emerged with most of the five scoring below the median of the generally low performance level of the index groups. The most striking association ($p=0.1$) was found in the same tests which were previously emphasized in the index group as showing a visuomotor defect in central neuro-integration, viz. Human Figure Drawing, Bender Visual Motor Gestalt Test and Pattern Completion, of the New South African Individual Scale tests the one most closely associated with visuo-motor perception.

The term "atrophy" used to describe these CT changes implies a wasting or shrinkage of a previously normal structure. An alternative preferred explanation is that the minimal changes seen at a variety of sites with no anatomical consistency on the scan may reflect a more severe form of suboptimal brain development with smaller gyri and wider sulci. Clearly there is no atrophy severe enough to produce ventricular dilatation or enlargement of the subarachnoid space. Nor is there any evidence of other organic brain damage.

The normal size of the ventricles and subarachnoid space support the concept that head circumference can be used as a maesure of brain size, allowance being made for skull and scalp thickness.

The normal ventricular size is in agreement with Valquist *et al.* (1971) who, using echoencephalography, found no increase in ventricular size in marasmic infants. As only marasmic infants were originally selected for our index group, no comment or comparison can be made with their finding of increased ventricular size in children with kwashiorkor.

Acknowledgments

We wish to thank the South African Medical Research Council for financial support, Miss A. Moodie whose help in collecting the subjects made this study possible, and Miss Bowie for her help with X-rays.

REFERENCES

Brown, R. E., 1965. Decreased brain weight in malnutrition and its implications. *East African Medical Journal, 42,* 582.

Monckeberg, F., 1975. In *Brain Function and Malnutrition: Neuropsychological Methods of Assessments.* Ed. by J. W. Prescott, M. S. Read and D. B. Coursin (John Wiley and Sons, New York, London), p. 25.

Stoch, M. B. and Smythe, P. M., 1963. Does undernutrition during infancy inhibit brain growth and subsequent intellectual development? *Archives of Disease in Childhood, 38,* 546.

1967. The effect of undernutrition during infancy on subsequent brain growth and intellectual development. *South African Medical Journal, 41,* 1027.

1976. Fifteen year developmental study on effects of severe undernutrition during infancy on subsequent physical growth and intellectual functioning. *Archives of Disease in Childhood, 51,* 327.

Valquist, B., Engsner, G. and Sjögren, I., 1971. Malnutrition and size of the cerebral ventricles. *Acta Paediatrica Scandinavica, 60,* 533.

Winick, M. and Rosso, P., 1969. Head circumference and cellular growth of the brain in normal and marasmic children. *Journal of Pediatrics, 74,* 774.

1981, *British Journal of Radiology*, 54, 955–960 NOVEMBER 1981

The role of abdominal computed tomography in lymphoma following treatment

By *G. Blackledge, M.R.C.P., †H. Mamtora, F.R.C.R., *D. Crowther, Ph.D., F.R.C.P., †I. Isherwood, F.R.C.R. and †J. J. K. Best, F.R.C.R.

*CRC Department of Medical Oncology, Manchester University and Christie Hospital & Holt Radium Institute, Wilmslow Road, Manchester M20 9BX and
†Department of Diagnostic Radiology, University of Manchester, Stopford Building, Manchester

(*Received April 1981*)

ABSTRACT

Two hundred and six patients with biopsy-proven lymphoma, 74 with Hodgkin's disease and 132 with non-Hodgkin's lymphoma had abdominal computed tomography for assessment of remission status (108 patients) or for investigation of relapse (98 patients). In 43 patients with diffuse large cell lymphomas scanned at a time of apparent complete remission CT was abnormal in 21. Sixteen of these patients have relapsed and died. Only one patient has relapsed in the group who have normal CT scans. This difference was significant ($p = 0.00001$). This difference was not seen in nodular lymphomas. There were very few patients with Hodgkin's disease in whom the CT scan was abnormal and there is a suggestion that many abnormalities following treatment may represent inactive Hodgkin's disease or fibrosis only. CT played a major role in diagnosing the full extent of relapse in both non-Hodgkin's lymphoma and Hodgkin's disease. Over 50% of the abnormal sites detected by CT would not have been shown by any other non-invasive investigation.

Five patients with treated Hodgkin's disease who had "B" symptoms only suggesting relapse were all shown by CT to have extensive intra-abdominal disease.

The introduction of whole-body computed tomography (CT) in 1975 provided a new non-invasive technique for the assessment of patients with lymphoma. Since then many authors have reported their experience with CT in the staging of lymphoma, especially Hodgkin's disease (Alcorn *et al.*, 1977; Best *et al.*, 1978; Breiman *et al.*, 1978; Jones *et al.*, 1978; Blackledge *et al.*, 1979, 1980a; Earl *et al.*, 1980). The majority of these studies concluded that CT was as good as or superior to lymphography for the assessment of retroperitoneal nodal disease. The accuracy of CT in detecting intra-abdominal disease, however, has been disappointing when compared to laparotomy, mainly because of its poor ability to detect splenic disease. As detection of splenic disease is important in the staging of lymphoma, especially Hodgkin's disease, CT has limitations as an initial staging investigation.

During follow up of patients with lymphoma, the requirements of a staging investigation are different. Assessment of remission is important, since in both Hodgkin's disease (HD) and many histological subtypes of non-Hodgkin's lymphoma (NHDL) achievement of complete remission is an important prognostic factor (Fisher *et al.*, 1977; Sutcliffe *et al.*, 1978b; Blackledge *et al.*, 1980b). The use of whole abdominal CT may reveal the presence of residual disease following treatment, and accurate assessment of the full extent of relapse may be of value in deciding choice of treatment.

If CT could be shown to be useful in these two important aspects of follow-up, namely relapse and remission assessment, then it would make a valuable contribution to the management of patients with lymphoma. The purpose of this investigation has been to determine the role of CT during follow-up of lymphoma patients in terms of remission assessment, detection of relapse and restaging at a time of relapse.

PATIENTS AND METHODS

Two hundred and six patients, 74 with HD and 132 with NHDL were scanned between September 1976 and December 1979 in the Department of Diagnostic Radiology, University of Manchester. All patients were managed and referred by members of the Manchester Lymphoma Group and had a biopsy-proven diagnosis of lymphoma, classified using the Rye nomenclature for HD (Lukes and Butler, 1966) or the modified Rappaport system for NHDL (Rappaport, 1966). Those patients with nodular pathology NHDL or diffuse well-differentiated lymphocytic pathology were regarded as having grade 1 pathology and received treatment as shown in Table I. Other cases of NHDL were regarded as having grade 2 pathology and received more intensive treatment (Table I). The treatment for patients with HD is also shown in Table I.

Assessment by CT and conventional investigations was made as follows.

1. *Remission assessment*

(i) HD. CT was performed within two months of completion of chemotherapy on those patients who showed evidence of intra-abdominal disease at presentation.

TABLE I

Treatment summary of patients with Hodgkin's disease and non-Hodgkin's lymphoma

HD	
I & II	Mantle radiotherapy with or without adjuvant chemotherapy (MVPP—6 courses)
III & IV	MVPP to remission plus 6 further courses. Radiotherapy to sites of bulky disease (MVPP—see Sutcliffe *et al.*, 1978b).
NHDL	
Favourable pathology	
I & II	Radiotherapy with or without adjuvant chemotherapy
II abdo	
III & IV	CVP chemotherapy (minimum 6 courses) radiotherapy to bulky disease (Bagley *et al.*, 1972)
Unfavourable pathology	
I & II	Radiotherapy with either VAP chemotherapy or C MOPP—6 courses
II abdo III & IV	VAP (6 weeks) plus radiotherapy to sites of bulky disease. Oral maintenance treatment for 2 years (Blackledge *et al.*, 1980b)

TABLE II

Findings by CT in patients with Hodgkin's disease in clinical remission

No. of patients scanned	26
Normal	20
Areas abnormal by CT	
Para-aortic nodes	2
Iliac nodes	2
Splenic hilar nodes	1
Liver	1
Spleen	1
No. of patients relapsing with abnormal CT scans	2/6
No. of patients relapsing with normal CT scans	1/20

(ii) NHDL. In the group with grade 1 pathology, CT was performed on completion of CVP therapy (Bagley *et al.*, 1972), usually between six and nine months from starting treatment. The group with grade 2 pathology had a CT scan between one and three months following completion of VAP treatment (Blackledge *et al.*, 1980b). When the scan was abnormal and the patient remained well, the examination was repeated from 8 to 36 months later.

The other investigations that were performed at remission assessment included haematological examination with bone marrow aspirate and trephine, liver function tests and plain chest radiograph. Lymphography was not routinely repeated, but if a lymphogram had been performed at presentation a plain abdominal radiograph was obtained to check the status of the opacified nodes. Any other investigation which had been performed at presentation and was abnormal was repeated. Complete remission was defined as the disappearance of all disease clinically and the return to normal of the results of all investigations which had been performed.

2. *Relapse assessment*

CT scans were performed to assess extent of relapse in the following situations:

(i) when there was clinical evidence of relapse with either nodal or extra-nodal disease;

(ii) when investigations suggested relapse, *e.g.*, abnormal liver function tests;

(iii) when a patient with Hodgkin's disease had "B" symptoms, but no other clinical signs of relapse. If relapse was detected by any means, appropriate treatment was given, depending upon the histology and distribution of disease.

Preparation of the patient, scanning technique and criteria for assessment of lymph node enlargement were as described previously (Best *et al.*, 1978).

Results

1. *Assessment of remission status*

In this study 108 patients (26 with HD and 82 with NHDL) were given a remission assessment, including CT. All patients were in apparent clinical remission, using the criteria described under "Patients and methods".

(i) *Hodgkin's disease.* The 26 patients scanned had evidence of intra-abdominal disease prior to treatment and the results are shown in Table II. There were seven areas in six patients which were regarded as abnormal. In the patient with two abnormal lymph node areas (para-aortic and left common iliac groups), clinical relapse occurred four months later in those areas. One other patient with iliac node involvement detected by CT also relapsed. Both patients achieved a second remission with combination chemotherapy. A further patient with a normal CT scan relapsed one month following assessment, with an enlarged liver and abnormal liver function tests. This patient responded satisfactorily to chemotherapy and is in complete remission two and a half years following initial assessment.

(ii) *NHDL.* Eighty-two patients with NHDL in apparent clinical remission were scanned; 39 had grade 1 (nodular histology) and 43 had grade 2 (diffuse histology). The results are shown in Tables III and IV. In grade 2 pathological group a normal abdominal CT scan was associated with continued relapse-free survival ($p=0.00001$) (Table III). In

TABLE III

CT SCAN RESULTS IN PATIENTS WITH DIFFUSE PATHOLOGY NON-HODGKIN'S LYMPHOMA IN APPARENT CLINICAL REMISSION USING CONVENTIONAL RESTAGING METHODS
(Follow up 15–60 months, median 36)

	Alive and well	Relapsing	Total
CT normal	21	1	22
CT abnormal	5	16	21
Total	26	17	43

$p = 0.00001$.

TABLE IV

CT SCAN RESULTS IN PATIENTS WITH NODULAR-PATHOLOGY NON-HODGKIN'S LYMPHOMA IN APPARENT CLINICAL REMISSION USING CONVENTIONAL RESTAGING METHODS
(Follow up 16–60 months, median 35)

	Alive and well	Relapsing or died	Total
CT normal	16	2	18
CT abnormal	14	7	21
Total	30	9	39

$p = 0.207$.

the five cases where CT was abnormal but patients are surviving, three out of five of the scans were performed within two months of complete clinical remission. Repeat scans in two of these patients, nine and 12 months later, showed regression in the previously abnormal areas.

In patients with nodular lymphoma the results were different (Table IV).

Abnormalities seen on CT were not necessarily associated with subsequent clinical relapse. There was no significant difference in relapse-free survival between patients with normal and abnormal CT scans ($p = 0.207$). Of the patients in this group who remain alive and well, 17 out of the 19 abnormal areas detected by CT were in nodal sites and only two in extra-nodal sites. However, of 13 abnormal areas detected in patients who subsequently relapsed, only six were in nodes and seven were in extra-nodal sites.

2. *Investigation of relapse*

(i) *HD*. Forty-eight patients with biopsy-proven HD were scanned at a time of relapse or suspected relapse. Twenty had clinical evidence of disease above the diaphragm only. Twenty-three had evidence of relapse below the diaphragm and eight had widely disseminated disease. There were five patients in whom only "B" symptoms suggested relapse.

TABLE V

CT FINDINGS IN 48 PATIENTS WITH RELAPSING HODGKIN'S DISEASE

Normal	8
Areas involved	
Nodes	
Para-aortic	28
Coeliac	8
Iliac	8
Mesenteric	3
Retro-crural	11
Splenic hilar	7
Liver	6
Spleen	5
Renal	3
Bone	2
Ascites	3
Unexpected findings	24

The CT findings in these patients are shown in Table V. In eight patients the abdominal scans were normal; six of them had evidence of relapse above the diaphragm only. The other two had enlarged inguinal nodes. The remaining 40 patients all had evidence of intra-abdominal disease documented by CT. The para-aortic node areas were most often involved; of the 11 patients with retro-crural lymphadenopathy, nine had also para-aortic node enlargement, and of the eight patients with coeliac node involvement, seven had para-aortic node enlargement. In four patients with splenic hilar node enlargement, the spleen was also enlarged. In two cases bone disease within a vertebra was seen, and there were three patients with renal or juxta-renal disease. Of the 20 cases who had clinical relapse above the diaphragm only, CT showed infradiaphragmatic disease in 14.

Additional unsuspected disease was found in 12 of 23 cases with infradiaphragmatic or generalized relapse. All five patients with "B" symptoms as the only clinical evidence of disease had abnormalities below the diaphragm on CT.

(ii) *NHDL*. CT was performed in 50 patients with NHDL at a time of relapse or suspected relapse. Of the 23 patients with grade 1 pathology, five had normal CT scans and four of the 27 with grade 2 pathology had normal examinations (Table VI). In four patients CT did not confirm the clinical suspicion of generalized disease within the abdomen; in ten, CT demonstrated abdominal disease, indicating that an apparently localized relapse was generalized.

Abnormal areas detected by CT are shown in Table VII. About twice as many areas were detected by CT as were expected from conventional clinical restaging assessment (excluding lymphography). All but three of the 15 retro-crural abnormalities were unsuspected clinically; in the three cases where relapse was suspected, involvement of the retro-crural nodes was seen as a paravertebral shadow on chest radiographs. Coeliac and mesenteric lymphadenopathy was rarely suspected on conventional re-restaging, and yet was present in 19 cases; in none, however, was coeliac or mesenteric node enlargement the only sign of abdominal disease.

In one case from the grade 2 pathology group in whom liver disease was unsuspected, a generalized increase in hepatic density was noted on CT. Nodules in the spleen were seen in one patient only; in all other cases with splenic involvement, relapse was documented by splenic enlargement only.

Abnormalities detected in other areas fall into three main groups: (1) pulmonary: seven abnormalities were seen in the lower lung fields on CT, but they were all visible on conventional radiography; (2) renal infiltration or obstructive uropathy due to lymphadenopathy in three patients; (3) bone involvement in two cases only.

TABLE VI

Number of patients relapsing with non-Hodgkin's lymphoma studied by CT

	Diffuse histology	Nodular histology
Total scanned	27	23
CT scan normal	4	5
CT changed diagnosis from generalized to localized relapse	2	2
CT changed diagnosis from localized to generalized relapse	6	4

Discussion

Improvements in radiotherapy and chemotherapy in the past two decades have resulted in dramatic changes in the prognosis of patients with HD; although approximately 80% of patients with advanced HD achieve clinical remission with combination chemotherapy, half will relapse within five years. If relapse occurs within one year of treatment with combination chemotherapy, the subsequent prognosis is poor (Sutcliffe *et al.*, 1980). Prognosis in HD is dependent on factors such as anatomical distribution of disease, extent of disease and systemic symptoms. Following treatment, assessment of whether remission is complete is important as patients who do not respond or who have an incomplete remission have a very poor prognosis (Sutcliffe *et al.*, 1978b). In some patients with advanced diffuse histiocytic lymphoma, long-term survival is achieved following combination chemotherapy and if the remission is complete, the incidence of relapse falls rapidly with time (DeVita *et al.*, 1975). Therefore the presence of residual disease following chemotherapy is of particular importance in the management of both HD and NHDL.

Accurate documentation of remission using conventional staging procedures, including lymphography, may underestimate the presence of disease. Using abdominal lymphography only, the nodes in the lower para-aortic and iliac areas are regularly opacified and the upper para-aortic, retro-crural, coeliac and splenic hilar regions cannot be assessed adequately. Using one node area or selected node

TABLE VII

Abdominal sites involved in patients with relapsing non-Hodgkin's lymphoma as seen by CT (50 patients)

	Nodular histology		Diffuse histology	
	Clinically		Clinically	
	Expected	Unexpected	Expected	Unexpected
Areas involved				
Retro-crural node	0	7	3	5
Para-aortic node	13	7	6	7
Iliac nodes	9	3	7	1
Coeliac nodes	0	5	0	4
Mesenteric nodes	1	5	0	4
Liver	6	3	5	1
Spleen	5	4	4	3
Splenic hilar node	0	1	0	1
Other area	4	3	7	0
Total	38	38	32	26

areas to monitor disease is likely to be unreliable because of different rates of response depending upon the bulk of disease and site within the body. Sutcliffe *et al.* (1978a) assessed complete remission by laparotomy following treatment, but this carries an appreciable risk of morbidity in immunosuppresed but potentially cured patients. CT, despite its limitations in the staging of disease, is a useful technique for mapping out the extent of nodal involvement in the whole abdomen and provides the baseline against which response to treatment may be assessed using serial examinations.

In the study of patients with HD scanned at apparent complete remission the presence of nodal enlargement in the para-aortic and iliac areas was associated with subsequent relapse in some patients. CT was useful in these patients as further chemotherapy enabled complete remission to be achieved. Reports from some centres suggest that para-aortic and iliac node involvement carried a worse prognosis when compared with either splenic disease or upper abdominal disease (Desser *et al.*, 1977; Stein *et al.*, 1979; Hoppe *et al.*, 1979). It is significant, however, that the number of patients who relapsed in this study is small and that there were also some patients who had evidence of nodal enlargement but who have not as yet relapsed. Since completion of this study, CT has been used routinely for remission assessment of patients who had abdominal HD at presentation. There have been two cases in whom CT suggested enlarged para-aortic nodes following treatment; in both cases, following second-look laparotomy, residual fibrous tissue only was found with no evidence of active HD. These cases confirmed the findings of Sutcliffe *et al.* (1978a) that residual abnormalities following treatment of Hodgkin's disease do not necessarily represent active HD. If no change is detected on follow-up scans and if other parameters are normal, then remission may be assumed. When there is doubt about the complete remission, however, biopsy of such nodes under ultrasound or CT control might be of value; such procedures would only be useful, however, when a positive biopsy is obtained.

In patients with grade 2 histology NHDL in apparent clinical remission an abnormal CT scan following treatment was clearly associated with poor prognosis and our results indicate that this group should receive further intensive treatment until the scan returns to normal. The presence of scan abnormality in the grade 1 histology group and its lack of significant association with prognosis in the small group studied is interesting and suggests that an abnormal scan may be followed without further treatment when residual abnormalities are confined to lymph nodes; however, further studies are required before definite treatment policies can be formulated and follow-up examinations would certainly be required to establish continuing regression. The ability of CT to demonstrate occult abdominal disease in patients with clinically complete remission may be useful in predicting the subsequent course of the disease; an abnormal CT scan may prove to be an important prognostic indicator for survival in patients with grade 2 histology and may indicate when further therapy is necessary.

Relapses in HD, if they occur, almost always become apparent in the first five years following initial treatment. Most relapses occur within the first 18 months and Weller *et al.* (1976) found that 87% of relapses occurred within the first three years. CT has the advantage of being able to detect disease in sites which remain undetectable on lymphography, and has fewer hazards. In the HD group, relapse was commonly seen in the para-aortic nodes and CT clearly showed more extensive involvement than suggested by clinical assessment. Of the 20 cases who had clinical relapse above the diaphragm, 14 (almost 75%) had evidence of sub-diaphragmatic disease on CT. Of particular importance was the detection of disease below the diaphragm in patients with "B" symptoms as the only clinical evidence of relapse. Of the 48 relapsed patients with HD, there were 31 patients in whom CT revealed disease which was not detected otherwise; in only seven areas of relapse in these patients did the disease occur in lymph nodes which could have been opacified at lymphography, and the remainder had disease documented by CT in areas such as coeliac nodes, retro-crural and splenic hilar nodes which would not be adequately assessed by lymphography. The measurement of regression in these areas allows assessment of treatment response and documentation of second remission to be made by CT.

Similarly, in the group with NHDL, CT was of value in the documentation of disease in clinically inaccessible areas (retro-crural, coeliac or mesenteric nodes). Of the patients with para-aortic disease almost half were clinically unexpected. Lymphography was not performed routinely in this group as a relapse investigation, but it is likely that of the 50 unexpected lymph node areas shown to be enlarged on CT, lymphography would have detected only 23% of the abnormalities, these being in the iliac or lower para-aortic regions.

In conclusion our results indicate that CT is useful in both HD and NHDL to document remission and delineate extent of disease in patients with relapse or suspected relapse. In the non-Hodgkin's lymphomas with grade 2 histology, the presence of residual disease was significantly associated with a poor prognosis, but no such correlation existed in the patients with grade 1 histology. An abnormal CT scan may prove to be an important prognostic indicator for survival. Larger studies are required to confirm this and the role of CT in predicting the course of the disease.

ACKNOWLEDGMENTS

Grateful acknowledgment is made to the members of the Manchester Lymphoma Group for allowing us to study patients in their care, and to Mrs. Eileen N. Morgan for secretarial assistance.

REFERENCES

Alcorn, F. A., Mategrano, V. C., Petasnick, J. P. and Clark, J. W., 1977. Contribution of computed tomography in the staging and management of malignant lymphoma. *Radiology, 125,* 717–723.

Bagley, C. M., DeVita, V., Berard, C. and Canellos, G. P., 1972. Advanced lymphosarcoma: intensive cyclical combination chemotherapy with cyclophosphamide, vinchristine and prednisome. *Annals of Internal Medicine, 76,* 227–234.

Best, J. J. K., Blackledge, G., Forbes, W. St. C., Todd, I. D. H., Eddleston, B., Crowther, D. and Isherwood, I., 1978. Computed tomography of the abdomen in staging and clinical management of lymphoma. *British Medical Journal, ii,* 1675–1677.

Blackledge, G., Best, J. J. K. and Crowther, D., 1979. The role of computed tomography in the staging and management of gastro-intestinal lymphoma. *Journal of the Royal Society of Medicine, 72,* 818–822.

Blackledge, G., Best, J. J. K., Crowther, D. and Isherwood, I., 1980a. Computed tomography in the staging of patients with Hodgkin's disease: a report on 136 patients. *Clinical Radiology, 31,* 143–147.

Blackledge, G., Bush, H., Chang, J., Crowther, D., Deakin, D., Dodge, O., Garrett, J., Palmer, M., Pearson, D., Scarffe, J., Todd, I. and Wilkinson, P., 1980b. Intensive combination chemotherapy with vincristine, adriamycin and prednisolone (VAP) in the treatment of diffuse histology non-Hodgkin's lymphoma: (a report of 89 cases with extensive disease from the Manchester Lymphoma Group). *European Journal of Cancer, 16,* 1459–1468.

Breiman, R. S., Castellino, R. A., Harell, G. S., Marshall, W. H., Glatstein, R. and Kaplan, H. S., 1978. CT-pathologic correlations in Hodgkin's disease and non-Hodgkin's lymphoma. *Radiology, 126,* 159–166.

Desser, R. K., Golomb, H. M., Ultmann, J. E., Ferguson, D. J., Moran, E. M., Griem, M. I., Vardiman, J., Miller, B., Oetzel, N., Sweet, D., Lester, E. P., Kinzie, J. and Blough, R., 1977. Prognostic classification of Hodgkin's disease in pathologic stage III. Based on anatomic considerations. *Blood, 49,* 883–893.

DeVita, V. T., Canellos, G. P., Chabner, B., Schein, P., Hubbard, S. P. and Young, R. C., 1975. Advanced DHL —a potentially curable disease. *Lancet, i,* 248–250.

Earl, H. M., Sutcliffe, S. B. J., Kelsey Fry, I., Tucker, A. K., Young, J., Husband, J., Wrigley, P. F. M. and Malpas, J. S., 1980. Computerised tomographic abdominal scanning in Hodgkin's disease. *Clinical Radiology, 31,* 149–153.

Fisher, R. I., DeVita, V. T., Hubbard, S. M. and Young, R. C., 1977. Prolonged disease-free survival in Hodgkin's disease following re-induction with MOPP. *Proceedings of the American Association of Cancer Research and ASCO, 18,* 318.

Hoppe, R. T., Cox, R. S., Rosenberg, S. A. and Kaplan, H. S., 1979. Prognostic factors in pathologic stage (PS) IIIA Hodgkin's disease (HD). *Proceedings of American Association for Cancer Research* and *American Society for Clinical Oncology,* March 1979, C-576.

Jones, S. E., Tobias, D. A. and Waldman, R. S., 1978 Computed tomographic scanning in patients with lymphoma. *Cancer, 41,* 480–486.

Lukes, R. J. and Butler, J. J., 1966. The pathology and nomenclature for Hodgkin's disease. *Cancer Research, 26,* 1063–1081.

Rappaport, H., 1966. Tumours of the haemopoietic system. In *Atlas of Tumor Pathology.* Section 3, Fascicle 8 (US Armed Forces Institute of Pathology, Washington, DC).

Stein, R. S., Golomb, H. M., Ultmann, J. E., Wiernick, P. H., Diggs, C., Hellman, S. and Mauch, P., 1979. Anatomic substages of stage III Hodgkin's disease (HD): a collaborative study. *Proceedings of American Society of Clinical Oncology, 20,* 438.

Sutcliffe, S. B., Economopoulos, T., Wrigley, P. F. M., Stansfield, A. G. and Malpas, J. S., 1980. Prognosis of Hodgkin's disease; patients who fail to remit or who relapse after combination chemotherapy. *Clinical Oncology, 6,* 329–336.

Sutcliffe, S. B., Katz, D., Stansfield, A. G., Shand, W. S., Wrigley, P. F. M. and Malpas, J. S., 1978a. Post-treatment laparotomy in the management of Hodgkin's disease. *Lancet, ii,* 57–60.

Sutcliffe, S. B., Wrigley, P. F. M., Peto, J., Lister, T. A., Stansfield, D. G., Whitehouse, J. M. A., Crowther, D. and Malpas, J. S., 1978b. MVPP chemotherapy regimen for advanced Hodgkin's disease. *British Medical Journal, i,* 679–683.

Weller, S. A., Glatstein, E., Kaplan, H. S. and Rosenberg, S. A., 1976. Initial relapses in previously treated Hodgkin's disease. I. Results of second treatment. *Cancer, 37,* 2840–2846.

1981, *British Journal of Radiology*, *54*, 961–965 NOVEMBER 1981

Dosimetry of renal radiopharmaceuticals: the importance of bladder radioactivity and a simple aid for its estimation

By *T. Smith, Ph.D., *N. Veall, D.Sc., F.Inst.P. and †D. G. Altman, B.Sc.

*Radioisotopes Division and †Division of Computing and Statistics, Clinical Research Centre, Harrow, Middlesex HA1 3UJ

(*Received February 1981 and in revised form May 1981*)

ABSTRACT

The contribution from radioactivity in bladder contents to dose commitments to the embryo, ovaries, red marrow, kidney, bladder wall and total body has been estimated for various renal radiopharmaceuticals, assuming a bladder-voiding period of 3.5 h. For hippuran and GFR agents this contribution is 70–97% of the embryo dose and 50–93% of the ovary dose. The embryo dose exceeds the ovary dose by a factor of two or more. For the radiopharmaceuticals with no significant kidney retention, the surface dose to the bladder wall is higher, by more than an order of magnitude, than doses to other organs and is largely responsible for the effective dose equivalent exceeding the estimated whole-body dose by factors of up to 25.

Since the estimation of cumulated activity in bladder contents is necessary for bladder dosimetry, a nomogram based on a 3.5 h voiding period is presented as a convenient aid for this purpose.

With the increasing variety of radiopharmaceuticals used to study renal function and morphology, it is important, for purposes of internal dosimetry, to consider the relatively high cumulated bladder radioactivity inherent in such diagnostic procedures in view of the proximity of the bladder to various tissues at risk. Recent advances in physical dosimetry methods (Loevinger and Berman, 1976) allow estimation of dose commitments from this "source organ" to the bladder wall and other target organs, uncertainties associated with metabolic and physiological parameters such as urine flow rate and bladder voiding pattern usually being the main limitations on accurate dosimetry. The purpose of this paper is to determine the relative magnitude of the contribution from radioactivity in bladder contents to dose commitments to the embryo, ovaries, red marrow, kidney, bladder wall and total body following the administration of radiopharmaceuticals to measure effective renal plasma flow (ERPF) or glomerular filtration rate (GFR) or for renal imaging. A necessary part of this study is the estimation of the cumulated activity in bladder contents and, as a convenient aid for this purpose, we have developed a simple nomogram, assuming a 3.5 h bladder voiding period.

METHODS

Calculations of all doses, other than the dose to the bladder wall, were based on the MIRD formula (Snyder *et al.*, 1975):

$$\bar{D}_{\text{target}} = \Sigma \tilde{A}_{\text{source}} \cdot S_{\text{target} \leftarrow \text{source}}.$$

Values of cumulated activity in source organs ($\tilde{A}$, MBq, or μCi h) were estimated using simple metabolic models to describe the *in-vivo* behaviour of the administered renal radiopharmaceuticals. The models assume that the tracers undergo monoexponential removal from the total-body distribution space at rates determined by the known clearances of the radiopharmaceuticals in question. Thus GFR tracers are assumed to mix instantaneously within the distribution space and to be cleared, in the normal case, with a biological half time of 100 min and kidney transit time of 5 min. The respective values for hippuran are assumed to be 25 min and 4 min. Whilst these models are simplifications of the true tracer kinetics, in that the delay in distribution between the plasma and extravascular extracellular fluid is ignored, it has been assumed that this will not significantly affect the radiation dose estimates. In the case of the renal imaging agents ^{99}Tc$^{\text{m}}$ DMSA and ^{99}Tc$^{\text{m}}$ gluconate, published biokinetic data were used (Arnold *et al.*, 1975). The value of $\tilde{A}$ for bladder contents, however, depends not only on the assumed biokinetic model but also on the bladder-emptying period (t_v). Cloutier *et al.* (1973) have shown that for a radiopharmaceutical cleared mono-exponentially by renal function with biological rate constant λ_b and successive voidings at intervals t_v, the cumulated activity in bladder contents is the sum to infinity of a geometric series, and is given by

$$\tilde{A}_{\text{bl}} = fA_0 \left\{ \frac{1-e^{-\lambda_p t_v}}{\lambda_p} - \frac{1-e^{-(\lambda_p+\lambda_b)t_v}}{\lambda_p+\lambda_b} \right\} \frac{1}{1-e^{-(\lambda_p+\lambda_b)t_v}} \cdot \quad (1)$$

where λ_p is the radioactive decay constant and f is the fraction of the administered activity A_0 which is cleared by the kidneys and which in the present context has the value of 1.00.

Nomogram for estimation of $\tilde{A}_{\text{bl}}/A_0$

For convenience we have developed a nomogram derived from equation (1) using determinant analysis which allows rapid estimation of $\tilde{A}_{\text{bl}}/A_0$ for a

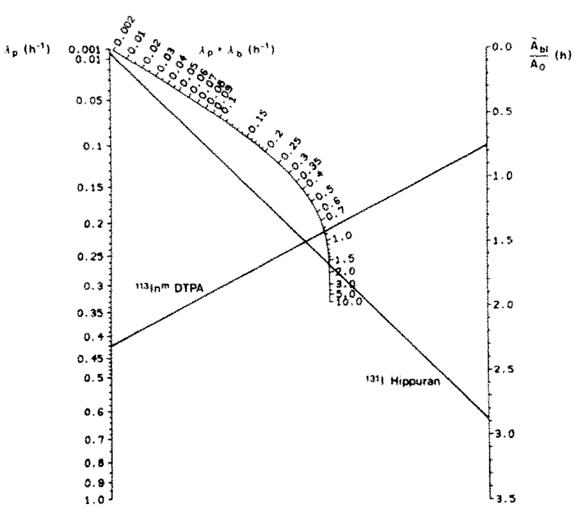


FIG. 1.

Nomogram to obtain the cumulated activity in bladder contents. $\tilde{A}_{\mathrm{bl}}/A_0$ (h per unit administered activity) from the biological (λ_b h^{-1}) and physical (λ_p h^{-1}) decay constants of an administered radiopharmaceutical which is cleared monoexponentially by the kidneys. Examples of its use for an ERPF agent (^{131}I-hippuran) and a GFR agent (^{113}In$^{\mathrm{m}}$ DTPA) are shown.

given t_v, and thus obviates manipulation of the cumbersome formula. The example shown in Fig. 1 is for a t_v of 3.5 h which we have taken as a representative bladder-emptying period (Syed, 1976). This shows that $\tilde{A}_{\mathrm{bl}}/A_0$ only approaches t_v when clearance is very fast (λ_b large) and that considerable benefit in radiation dose reduction from radioactivity in the bladder results from a reduction in λ_b and increase in λ_p. For example, the GFR agent ^{113}In$^{\mathrm{m}}$ DTPA has a short radioactive half-life (100 min) equal to its biological clearance half time ($\lambda_p = \lambda_b = 0.42$ h^{-1}) and the resultant $\tilde{A}_{\mathrm{bl}}/A_0$ is only 0.75 h per unit administered activity. On the other hand, for the longer-lived ^{131}I-hippuran ($\lambda_p = 0.0036$ h^{-1}) which is cleared more rapidly ($\lambda_b = 1.66$ h^{-1}), the value of $\tilde{A}_{\mathrm{bl}}/A_0$ is increased to 2.9 h per unit administered activity and thus approaches the bladder voiding period (3.5 h). Whilst we have used single exponential models for the above examples, the nomogram can be used with multicomponent models such as those which describe the whole-body retention of ^{99}Tc$^{\mathrm{m}}$ gluconate, the individual components being analysed separately.

Values of S (Gy/MBq s or rad/μCi h) for all target organs other than the embryo and bladder wall were taken from tables (Ford, 1980) which have been updated from those of MIRD Pamphlet 11 (Snyder *et al.*, 1975) for use in the derivation of the data given in ICRP 30 (1979) and which will presumably be published in due course. Values of S for the embryo as target organ were taken from tables given by Smith and Warner (1976) or calculated from physical output data (Watson, 1980) and tables of γ-ray absorbed fractions (Smith and Warner, 1976). The value of S for bladder contents as source organ is based on a fixed volume of 200 ml and thus takes no account of the variation in the dose rate to the bladder wall due to the changing volume of bladder contents. We have therefore calculated doses to the bladder wall on the basis of the bladder model of Snyder and Ford (1976) which allows the estimation of dose rates for different volumes of bladder contents, followed by integration over the filling cycle. For this purpose, the urine flow rate (1400 ml d^{-1}) of Reference Man (ICRP, 1975) was used. For non-penetrating radiation, we have adopted the same approach as that used by the Medical Internal Radiation Dose Committee (Snyder *et al.*, 1975) and calculated a surface dose to the bladder wall on the assumption that this is half the average dose to the bladder contents. For target organs other than the bladder wall and for bladder contents as the source organ, S values based on a fixed 200 ml bladder content were used.

Estimation of the effective dose equivalent

Except for ^{99}Tc$^{\mathrm{m}}$ DMSA, radiation doses to target organs were calculated using three source organs, namely kidneys, bladder contents and total body, where the cumulated activity of the latter excludes that in kidneys and bladder contents. For calculating the effective dose equivalent (ICRP 26, 1977; Sowby, 1978), the target-organ doses used were those for the six organs listed in ICRP 26, namely gonads, breast, red bone marrow, lungs, thyroid and bone surfaces, together with the doses to kidneys, bladder wall and total body. The gonad dose was taken as the mean of the doses to ovaries and testes, and the dose to breast was assumed to be the same as that to muscle. Kidneys and bladder wall were used as two of the five organs in the "remainder" (ICRP 26) with weighting factors of 0.06 and, in the absence of other organ doses significantly higher than the total body dose, three further arbitrary organs with weighting factors of 0.06 were assumed to receive the same dose as the total body. In the case of ^{99}Tc$^{\mathrm{m}}$ DMSA, liver and spleen were used as both source and target organs in addition to those given above, and the total body dose was used to represent that of the fifth outstanding organ of the "remainder".

RESULTS

Table I lists the radiation dose commitments (μGy per administered MBq) to the embryo, ovaries, red marrow, kidneys, bladder wall and total body for a number of renal radiopharmaceuticals. Doses to the testes were on average two thirds of the doses to the ovaries. The proportions of the organ doses which are due to the contribution from radioactivity in bladder contents (for a 3.5 h voiding period) are also shown. An estimate of the effective dose equivalent is given in the final column of Table I together with the magnitude of the bladder wall contribution to this value.

DISCUSSION

The nomogram described above is a convenient aid for calculating cumulated activity in bladder contents and is sufficiently accurate in practice in view of the various assumptions such as filling rate and voiding period on which the present bladder model is based.

The results in Table I have been calculated for normal renal function, when the radioactivity in bladder contents has its largest influence on dosimetry. The importance of this contribution is evident, though for the renal-imaging radiopharmaceuticals ^{99}Tc^{m} DMSA and ^{99}Tc^{m} gluconate, kidney retention of tracer reduces the bladder effect. Apart from its obvious influence on the bladder-wall dose, the contribution from bladder radioactivity to the embryo dose is also particularly marked, being about 96% for hippuran and 85% for most GFR agents. Whilst these contributions are calculated for a 3.5 h bladder-voiding period, they are so large that the effect of bladder radioactivity remains predominant for even more frequent voiding.

Our results show that for the particular kinetic data we have used here the radiation doses to the embryo are about double those to the ovaries and thus confirm the conclusions of Husak and Wiedermann (1980) that, in early pregnancy, the radiation dose to the embryo cannot be approximated by that to the ovaries. Except for radiopharmaceuticals partly retained by the kidney, the dose to the surface of the bladder wall in normal subjects is much higher than that to any other target organ, often by more than an order of magnitude. This has considerable bearing on the calculation of effective dose equivalents which, for all the radiopharmaceuticals considered, exceed the actual total-body dose by factors of 4 to 25. The higher factors are observed

TABLE I

CONTRIBUTIONS FROM BLADDER RADIOACTIVITY TO VARIOUS TARGET-ORGAN DOSES FOR RENAL RADIOPHARMACEUTICALS BASED ON A 3.5 H BLADDER VOIDING PERIOD

	Dose (μGy/MBq) (% contribution from bladder radioactivity)						Effective dose equivalent (μSv/MBq)
Radiopharmaceutical	Embryo	Ovaries	Red marrow	Kidneys	Bladder wall	Total body	
^{131}I hippuran	40	17	4.9	30	2460	6.3	156
	(96)	(90)	(65)	(2.5)	(>99)	(74)	(95)
^{125}I hippuran	7.8	1.8	0.6	4.6	374	1.2	24
	(97)	(86)	(37)	(0.04)	(>99)	(79)	(95)
^{123}I hippuran	20	7.3	2.5	6.6	485	2.6	32
	(97)	(93)	(71)	(3.5)	(>99)	(81)	(90)
^{51}Cr EDTA	2.8	1.3	0.6	1.5	42	0.6	3.2
	(86)	(73)	(36)	(2.8)	(>99)	(46)	(79)
^{99}Tc^{m} DTPA	9.2	4.2	2.4	4.4	134	1.8	10
	(85)	(72)	(39)	(2.5)	(99)	(45)	(80)
^{111}In DTPA	37	17	7.9	15.6	466	7.1	36
	(86)	(75)	(38)	(3.1)	(99)	(49)	(77)
^{113}In^{m} DTPA	9.1	5.0	3.0	14.3	477	3.1	32
	(71)	(52)	(18)	(0.9)	(>99)	(27)	(88)
^{125}I iothalamate	6.7	2.3	1.8	6.5	230	1.8	16
	(83)	(52)	(10)	(0.03)	(>99)	(41)	(88)
^{140}La DTPA	162	85	35	132	4410	41	313
	(83)	(67)	(28)	(3.1)	(>99)	(41)	(85)
^{169}Yb DTPA	39	17	11	30	1070	8.5	74
	(84)	(68)	(31)	(1.0)	(>99)	(39)	(86)
^{99}Tc^{m} DMSA	5.4	3.7	6.3	185	37	4.0	17
	(39)	(22)	(4)	(0.02)	(95)	(5)	(13)
^{99}Tc^{m} gluconate	9.0	4.7	3.9	46	138	2.7	14
	(73)	(55)	(20)	(0.2)	(99)	(25)	(61)

for the ERPF and GFR agents, and the bladder-wall dose is shown to be very largely responsible. However, these effective dose-equivalent values may subsequently require qualification in two respects.

Firstly, there are reasons to suggest that a weighting factor of 0.06 may over-estimate the risk of detrimental effects due to irradiation of the bladder wall: if it should be decided that the weighting factor should be 0.03, like that for thyroid and bone-surfaces, this could result in an almost two-fold reduction in our estimates of effective dose equivalent based on a surface dose to the bladder wall.

Secondly, the difference between a surface dose to the mucosal cells and an average dose to the entire bladder wall can be considerable, especially for radionuclides such as $^{99}\mathrm{Tc^m}$ with large numbers of short range Auger and conversion electrons where the two dose estimates may differ by an order of magnitude (Snyder and Ford, 1976). However, it has been the policy of the ICRP to use surface dose rate extensively in the past, for example to estimate the dose to the walls of the gastrointestinal tract from radioactivity in the contents (ICRP 30, 1979).

Where data are directly comparable, our dose estimates are in good agreement with those reported elsewhere (Elliott *et al.*, 1976; O'Reilly *et al.*, 1977; Elliott and Britton, 1978; O'Reilly *et al.*, 1979; Husak and Wiedermann, 1980), and our higher estimates of bladder-wall doses are the result of making allowance for the effects of bladder-filling rate. Our estimate of bladder-wall dose for $^{99}\mathrm{Tc^m}$ DTPA is in good agreement with that of Diffey and Hilson (1976) who also made this allowance by a different technique.

The contributions from radioactivity in the bladder to the dose commitment of organs other than the bladder wall are directly related to the cumulated activity in bladder contents and, for the radiopharmaceuticals considered, are approximately in direct relation to the bladder-voiding period (t_V). There is, however, no such relationship for the bladder-wall dose because, whereas more frequent voiding tends to reduce this dose, the smaller average volumes of bladder contents tend to increase it. The net result, for the radiopharmaceuticals considered, is that a reduction in t_V from 3.5 to 1 h reduces the bladder-wall dose to only about two thirds of that for a 3.5 h void, assuming a constant flow-rate of urine.

It has been recommended by a working party of the former MRC Isotope Advisory Panel (Ellis *et al.*, 1977) that, except where radiopharmaceuticals are administered for research purposes, implementation of the ten-day rule need only be considered for those radiopharmaceutical investigations which will give rise to gonad doses in excess of 500 μGy (50 mrad) over a time which is short compared with ten days, although there is no general agreement on this figure. Whatever value of gonad dose is finally adopted for this purpose, it is evident that the dose from bladder contents could be a deciding factor for some renal imaging techniques. When radioactive material is to be administered for research purposes and it is necessary to obtain "informed consent", some quantitative estimate of the risk which can be expressed in everyday terms is necessary. The effective dose equivalent has been introduced as the best available basis for assessing risks to occupationally exposed workers and *faute de mieux* most workers faced with this problem will use this parameter when administering radiopharmaceuticals for research purposes. Whilst it is important to bear in mind that the present model possibly represents "worst case" estimates of the dose to the bladder wall, for reasons stated above, it is evident that it can be used to assess the value of procedures such as decreasing the voiding period which can reduce the effects of bladder radioactivity or for comparing the relative merits of different radionuclide labels for equivalent radiopharmaceuticals.

REFERENCES

Arnold, R. W., Subramanian, G., McAfee, J. O., Blair, R. J. and Thomas, F. D., 1975. Comparison of $^{99}\mathrm{Tc^m}$ complexes for renal imaging. *Journal of Nuclear Medicine*, *16*, 357–367.

Cloutier, R. D., Smith, S. A., Watson, E. E., Snyder, W. S. and Warner, G. G., 1973. Dose to the fetus from radionuclides in the bladder. *Health Physics*, *25*, 147–161.

Diffey, B. L. and Hilson, A. J. W., 1976. Absorbed dose to the bladder from $^{99}\mathrm{Tc^m}$ DTPA. *British Journal of Radiology*, *49*, 196–198.

Elliott, A. T. and Britton, K. E., 1978. A review of the physiological parameters in the dosimetry of ^{123}I and ^{131}I-labelled hippuran. *International Journal of Applied Radiation and Isotopes*, *29*, 571–573.

Elliott, A. T., Britton, K. E., Brown, N. J. G., Pearce, P. C., Smith, F. R. and Barnasconi, E. W., 1976. Dosimetry of current radiopharmaceuticals used in renal investigation. Proceedings of the Conference at Oak Ridge, Tennessee, April 26–29, 1976 (Bureau of Radiological Health, US Department of Commerce, HEW Publication 76-8044, Washington, DC), pp. 293–304.

Ellis, R. E., Nordin, B. E. C., Tothill, P. and Veall, N., 1977. The application of the "ten-day rule" in radiopharmaceutical investigations. *British Journal of Radiology*, *50*, 200–202.

Ford, M. R., 1980. Personal communication.

Husak, V. and Wiedermann, M., 1980. Radiation absorbed dose estimates to the embryo from some nuclear medicine procedures. *European Journal of Nuclear Medicine*, *5*, 205–207.

International Commission on Radiological Protection, 1975. Publication 23: *Report of the Task Group on Reference Man* (Pergamon Press, Oxford).

1977. Publication 26: Recommendations of the ICRP. *Annals of the ICRP*, *1*, 1–53 (Pergamon Press, Oxford).

1979. Publication 30: Limits for intakes of radionuclides by workers, *Annals of the ICRP*, 2 (Pergamon Press, Oxford).

LOEVINGER, R. and BERMAN, M., 1976. A revised schema for calculating the absorbed dose from biologically distributed radionuclides. Medical Internal Radiation Dose Committee, Pamphlet No. 1, Revised (Society of Nuclear Medicine, New York).

O'REILLY, P. H., HERMAN, K. J., LAWSON, R. S., SHIELDS, R. A. and TESTA, H. J., 1977. 123-iodine: a new isotope for functional renal scanning. *British Journal of Urology*, *49*, 15–21.

O'REILLY, P. H., SHIELDS, R. A. and TESTA, H. J., 1979. *Nuclear Medicine in Urology and Nephrology*. (Butterworths, London).

SMITH, E. M. and WARNER, G. G., 1976. Estimates of radiation dose to the embryo from nuclear medicine procedures. *Journal of Nuclear Medicine*, *17*, 836–839.

SNYDER, W. S. and FORD, M. R., 1976. Estimation of dose to the urinary bladder and to the gonads. Proceedings of Conference at Oak Ridge, Tennessee, April 26–29, 1976 (Bureau of Radiological Health, US Department of Commerce, HEW Publication 76–8044, Washington, DC), pp. 313–349.

SNYDER, W. S., FORD, M. R., WARNER, G. G. and WATSON, S. B., 1975. "S", Absorbed dose per unit cumulated activity for selected radionuclides and organs. Medical Internal Radiation Dose Committee, Pamphlet No. 11 (Society of Nuclear Medicine, New York).

SOWBY, F. D., 1978. The 1978 Stockholm Meeting of The International Commission on Radiological Protection. *Physics in Medicine and Biology*, *23*, 1209–1212.

SYED, I. B., 1976. Dosimetry of indium-113m radiopharmaceuticals with special attention to the urinary bladder. Proceedings of the Conference at Oak Ridge, Tennessee, April 26–29, 1976 (Bureau of Radiological Health, US Department of Commerce, HEW Publication 76–8044, Washington, DC), pp. 360–369.

WATSON, S. B., 1980. Personal communication.

Book review

Radionuclide Imaging Artefacts. By L. D. Wells and D. R. B. Bernier, pp. v+139, 1980 (Year Book Medical Publishers, Chicago/London), £11·75.
ISBN 0-8151-9217-7

As the authors say in the foreword, we profit and learn most from our mistakes. This book is a collection of mistakes: some in instrumentation, some introduced by the patient, some from peripheral devices added to the imaging chain, some in the preparation and administration of the radiopharmaceutical.

A number of contributors are acknowledged who have sent in examples of the many and various mishaps that can occur with radionuclide imaging. The authors discreetly left off the individual attribution. The net result is a valuable book which all those engaged in day to day nuclear medicine departments of imaging will profit from reading.

The contents are not indexed but set out in five main groups. Each illustrates the resulting image—or lack of it—with the minimum of text indicating the type of problem and its recognition and method of correction. This last is frequently the terse comment, "call service representative". A great many are in fact due to relatively minor problems which can be rectified by local hospital staff rather than requiring the instrument-makers' engineers. The very first example is a series of three pictures of cracked gamma camera crystals. This ultimate mishap will hopefully not have been seen by most radiographers and technicians in their own experience, and one is happy to learn from the problems of others! Further illustrations show examples of photomultiplier tube misbehaviour in a gamma camera head, X–Y distortion images, and pre-amplifier troubles. The second section deals with the accessory imaging devices—formatters and polaroid and similar cameras for obtaining a hard copy result. Many of these are of necessity rather linked to a particular make of camera or scanner, and its mode of action—or inaction. Nevertheless, they provide a valuable series of artefacts, useful teaching points for any department. The section on technical errors is larger: 36 examples varying from light leaks to contamination of the bed and from hot fingers to cold coins. These are of almost universal application. The related series in the fourth section of "patient-induced artefacts" illustrate the problems with movement, prostheses, and the almost infinite variety of self-contamination which patients find possible. A final short section gives just a few examples of artefacts due to problems with radiopharmaceutical preparation and administration.

The technicians in our own department found it both valuable and amusing. They were a little taken aback that the only remedy suggested for a technician's hot finger showing up on a brain scan was to restrain the patient in a different way! However, they were also able to produce a series of fascinating artefacts not illustrated in this book and I suspect many departments of radionuclide imaging would be interested to contribute to a second edition—even if anonymously. This small book can be thoroughly recommended for the coffee table in the radiographers' rest-room. It certainly serves as a reminder of the almost innumerable possibilities for artefact during radionuclide imaging and the need for constant care and attention to detail.

D. H. KEELING.

1981, *British Journal of Radiology*, 54, 966–968

The effect of photon absorption by breast tissue in myocardial imaging with thallium 201

By *H. Singh, M.R.C.P. and D. A. Causer, Ph.D.

Departments of Cardiology, and Clinical Physics & Bio-engineering, Walsgrave Hospital, Coventry

(*Received October 1980 and in revised form June 1981*)

ABSTRACT

The effect of overlying breast tissue on ^{201}Tl imaging of the myocardium has been studied experimentally and in two patients in whom normal images were only obtained after moving the breast out of the field of view.

Since its use for myocardial imaging was first suggested by Kawana *et al.* in 1970, ^{201}Tl has been used extensively for the study of patients with coronary artery disease. Thallium is taken up by myocardium in proportion to perfusion (Strauss *et al.*, 1975), so that areas of reduced activity on scans indicate local reduction of blood flow.

Several studies have demonstrated the correlation between perfusion defects on myocardial images and coronary artery disease assessed by angiography. The frequency with which normal scans occur in patients with coronary artery disease varies between studies (Bailey *et al.*, 1977; Blood *et al.*, 1978), but there is always a very low incidence of scan abnormalities in the absence of coronary artery disease (*e.g.* Ritchie *et al.*, 1977).

The reason for false positive scans has not been established. This report suggests one possible mechanism, based on thallium studies in two patients and *in-vitro* experiments on the physical properties of ^{201}Tl.

CASE REPORTS

Case 1

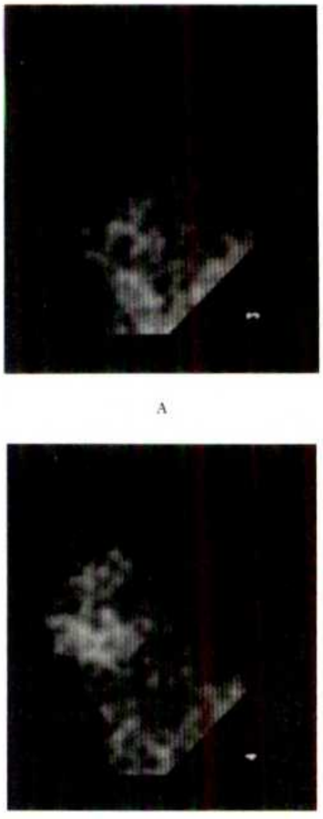
^{201}Tl imaging at rest and after exercise was performed on a 62-year-old woman presenting with grade three angina pectoris. The exercise study was undertaken first. The patient performed a symptom-limited exercise test on a bicycle ergometer and at the end-point (anginal chest pain) 55 MBq (1.5 mCi) of ^{201}Tl were injected intravenously and followed by a flushing injection of sterile saline. The patient was encouraged to continue exercising during and for 60 seconds after the injection.

Myocardial imaging was begun within eight minutes of injection, using an Elscint camera and a low energy, medium resolution collimator. The standard projections obtained were anterior, 45° left anterior oblique (LAO) and left lateral (LL). As was the custom in our department, the patient remained supine for all views, the camera head being rotated over the stationary patient.

Anterior and LAO images were satisfactorily obtained, but the LL image was inadequate in that no heart image could be readily identified. The patient was noted to have pendulous breasts such that in the LL image breast tissue was interposed between the chest wall and the gamma camera. The left breast was moved to the anterior chest wall and secured with adhesive tape. The LL view was immediately repeated and showed a striking improvement in the quality of the myocardial image (Fig. 1).

Case 2

The second patient was a 54-year-old woman who gave a two-year history of angina. Her symptoms had been gradually progressive despite treatment with beta-adrenergic blockade and in the last six months angina had occurred on


A

B

FIG. 1.

Superior left lateral thallium scans of Case 1, showing an improved myocardial image with the breast strapped away from the field of view. (A) anterior, unstrapped. (B) posterior strapped.

---

*Present address: The Hospital for Sick Children, Great Ormond Street, London WC1.

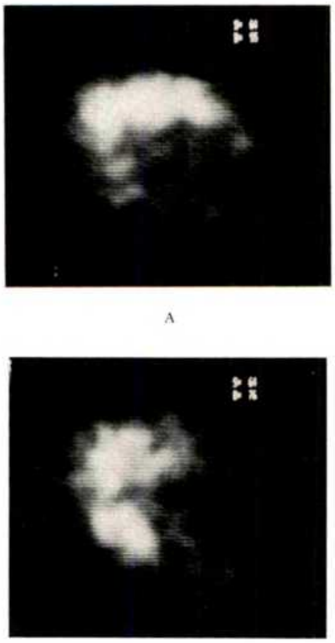
walking on the level. She initially underwent cardiac catheterization and coronary angiography with the following findings. The left ventricular angiogram was normal; the left main, right and circumflex arteries were also normal. There was a probable stenosis at the origin of the left anterior descending artery (LAD) and a further stenosis in the LAD just beyond the diagonal branch.

Exercise thallium studies were then performed as for Case 1. The anterior view was obtained satisfactorily, and when the LAO image was seen it showed a perfusion defect suggestive of a significant left circumflex artery (LCx) lesion. It was observed that in this view the left breast, which was less pendulous than in Case 1, was interposed between the chest wall and the gamma camera at the centre of the field of view. The breast was moved towards the mid-line anteriorly, and away from the gamma-camera field of view. The LAO view was then repeated immediately, with the patient positioned relative to the gamma camera exactly as for the first LAO image. It was apparent that there was a significant difference in the LAO views obtained before and after moving the left breast (Fig. 2).

DISCUSSION

Low-energy photons are heavily absorbed even in relatively low-density media such as breast tissue and water. The total attenuation coefficient for 75 keV photons in water is 0.18 cm^{-1} (75 keV is chosen as the peak of the X-ray spectrum from ^{201}Tl). The coefficient for such photons in breast tissue is 0.19 cm^{-1}, and so water can be used experimentally to simulate the effect of absorption by breast tissue.

The percentage penetration through 5, 10 and 15 cm of water predicted by the total attenuation coefficient is 40, 16 and 6% respectively, the figures applying to "narrow beam" conditions. That the theoretical penetration was applicable to our gamma-camera system was assessed by imaging a small ^{201}Tl source through air and then through 10 cm of water. The penetration through water was found to be 19.7%, which differs slightly from the predicted value (16%).


A

B

FIG. 2.

45° LAO myocardial images in Case 2, showing the effect of altering the position of the left breast. (A) inferior, unstrapped. (B) superior, strapped.

The difference is accounted for partly by scattering effects but also by the presence in the ^{201}Tl spectrum of X rays with energies between 65 and 82 keV, as well as higher-energy γ rays of low abundance. All these factors would tend to increase the measured penetration.

Figure 1 shows the LL images obtained in Case 1 with the breast unstrapped and then strapped. No quantitative analysis was undertaken, but qualitatively a much clearer myocardial image was obtained when the breast was strapped away from the gamma camera field of view.

Figure 2 shows the LAO image in Case 2. The perfusion defect which is obvious in the postero-lateral area of the left ventricular image is not apparent when the left breast is strapped away. Quantitative analysis of the two scans was undertaken using the computer light pen.

The myocardial image with the breast unstrapped was divided into five regions of interest; regions 1 and 2 were over the septum, region 3 over the apex and regions 4 and 5 over the postero-lateral wall. Counts per unit area were recorded for each region. The drawn regions were stored and then recalled to overlie the myocardial image obtained with the breast strapped away from the gamma-camera field of view. The new counts per unit area for each region were recorded.

For each LAO image, the region having the highest count density was designated as having a count of 100%, and the count density in other regions was expressed as a percentage of this. The results are shown in Table I. The absolute number of counts per region was of the order of 30000–40000, which resulted in a standard deviation of the count densities of about 0.5%.

It is apparent that shifting the breast led to a considerable change in the counts recorded in different regions. The most obvious change was in region 4, which showed the highest count density in the image with the breast strapped, but much less activity compared to the septal areas on the image with the breast unstrapped and in its normal position. The quantitative analysis confirmed the clinical impression of a perfusion defect seen only on

TABLE I

QUANTITATIVE ANALYSIS OF LAO IMAGES IN CASE 2. FOR EACH IMAGE, THE COUNTS ARE EXPRESSED AS A PERCENTAGE OF THOSE IN THE REGION WITH THE HIGHEST COUNT DENSITY. STANDARD DEVIATION OF THE COUNT DENSITIES IS APPROXIMATELY ½%

Region	Count density	
	Breast unstrapped	Breast strapped
1	95	88
2	100	97
3	92	90
4	86	100
5	83	88

the LAO image with the left breast in its normal position.

From the foregoing observations, it can be assumed that the penetration of thallium X rays through water is comparable to the penetration through breast tissue. As the myocardial-to-background ratio for thallium scanning is about 2:1, breast tissue of 5–10 cm thickness could cause sufficient photon absorption to reduce myocardial counts to background levels.

When breast tissue overlies the whole myocardium, a uniform reduction in counts because of absorption of photons will produce poor-quality thallium scans. We believe this to have occurred in the first patient, where an initial poor-quality scan was improved by moving the left breast.

When breast tissue only partly overlies the myocardium, unequal absorption of photons from the myocardium may give the appearance of a regional perfusion defect. From the angiographic findings in Case 2 a postero-lateral perfusion defect (indicative of a circumflex lesion) would not have been expected. That this defect was a "false positive" was shown by repeating the LAO view after moving the left breast.

Our conclusion is that false-positive perfusion defects may be obtained as a result of photon absorption by breast tissue. We would suggest that in thallium studies on women the left breast should be moved away from the field of view of the gamma camera. Where this is not possible, as in younger women with firm breast tissue, perfusion defects should be interpreted with caution.

ACKNOWLEDGMENTS

We are grateful to Dr. I. R. Gray and Mr. J. A. Dyde for allowing us to report on patients under their care, and to Miss S. E. Burnett for her secretarial expertise.

REFERENCES

BAILEY, I. K., GRIFFITH, L. S., ROULEAU, J., STRAUSS, H. W. and PITT, B., 1977. Thallium-201 myocardial perfusion imaging at rest and during exercise. Comparative sensitivity to electrocardiography in coronary artery disease. *Circulation, 55*, 79–87.

BLOOD, D. K., MCCARTHY, D. M., SCIACCA, R. R. and CANNON, P. J., 1978. Comparison of single dose and double dose thallium-201 myocardial perfusion scintigraphy for the detection of coronary artery disease and prior myocardial infarction. *Circulation, 58*, 777–788.

KAWANA, M., KRIZEK, H., PORTER, J., LATHROP, K. A., CHARLESTON, D. and HARPER, P. V., 1970. Use of Tl-199 as potassium analogue in scanning. *Journal of Nuclear Medicine, 11*, 333.

RITCHIE, J. L., TROUBAUGH, G. B., HAMILTON, G. W., GOULD, K. L., NARAHARA, K. A., MURRAY, J. A. and WILLIAMS, D. L., 1977. Myocardial imaging with thallium-201 at rest and during exercise. Comparison with coronary arteriography and resting and stress electrocardiography. *Circulation, 56*, 66–71.

STRAUSS, H. W., HARRISON, K., LANGAN, J. K., LEBOWITZ, E. and PITT, B., 1975. Thallium-201 for myocardial imaging. Relation of thallium-201 to regional myocardial perfusion. *Circulation, 51*, 641–645.

Book review

Gynaecological Radiology. By G. H. Whitehouse, pp. 240, 1981 (Blackwell, Oxford), £24·00.
ISBN 0-632-00726-5

It is a pleasure to welcome this book. It fills a gap, as no British book devoted to gynaecological radiology has been published since the second world war.

The first quarter of the book is given over to description and discussion of the conventional X-ray examinations by both plain and contrast techniques. There is then consideration of the radiological findings in disease, taken conventionally in groups: congenital, inflammatory, iatrogenic, tumours, etc. Succinct chapters on ultrasound and computed tomography by Dr. C. H. Wright of Abergele (late of St. Thomas', London and the University of Kansas) complete the book.

The substantial page size allows for a spacious display of the illustrations which are well-chosen and clearly show the relevant points. The hysterosalpingogram is particularly well covered. The text is common sense and deals in particular with common lesions. This is not an encyclopaedic comprehensive book but one of practical value to the radiologist particularly working with "conventional" techniques. The aggregation of ultrasound and CT scanning into separate sections has advantages, although many would prefer a discussion of all imaging modes together for each clinical problem. These sections on ultrasound and computed tomography are too short to review their role fully, but they do give an excellent overview of their capabilities.

The first part of the book should be considered as essential reading for the Part I Fellowship and the remainder for the Part II. Any department carrying out gynaecological radiology will wish to have it in their library.

J. G. B. RUSSELL.

1981, *British Journal of Radiology*, 54, 969–972 NOVEMBER 1981

Modification of the oral radiation death syndrome with combined WR–2721 and misonidazole*

By P. Grigsby, M.S. and Y. Maruyama, M.D.

Radiation Medicine Department, University of Kentucky Medical School, Lexington, Kentucky 40536, USA

(*Received February 1981*)

ABSTRACT

In order to investigate the combined use of radioprotective and radiosensitizing chemicals we have used WR–2721 and misonidazole to study their combined chemical toxicity and radiomodifying effects in our model using the oral radiation death (ORD) syndrome as the endpoint. Our data demonstrate that WR–2721 does protect against the ORD syndrome. Misonidazole does not sensitize the normal oral cavity to local irradiation. WR–2721 and misonidazole produce additive toxicity when injected simultaneously and the combination can provide an overall protective response to the ORD syndrome. We conclude that the combination may be potentially useful for the treatment of cancers of the oral cavity.

The oral radiation death (ORD) syndrome (Quastler *et al.*, 1956) occurs in the mouse when only the head and neck region are irradiated. This syndrome has been employed as our model for investigating the radioprotective ability of WR–2721 (S–2–(3–aminopropylamino)–ethylphosphorothioic acid) on the oral cavity structures of the mouse (Grigsby and Maruyama, 1980). A dose modification factor (DMF) of 2.1 has been achieved with WR–2721 in this model (Utley *et al.*, 1978). Other investigators have demonstrated a DMF of 2.5 by unilateral irradiation of the rat parotid gland in comparison with the irradiated autologous control (Sodicoff *et al.*, 1978).

The radiosensitizer misonidazole has been shown to sensitize effectively several tumour systems to the lethal effects of radiation without sensitizing normal tissues (Denekamp and Harris, 1975). In our studies, we have demonstrated that there is no sensitization of the oral cavity mucosa of the mouse, and a twofold increase in the mean survival time when the buccal mucosa is implanted with the EMT6/Ky tumour (Grigsby and Maruyama, 1980).

Since these two drugs, WR–2721 and misonidazole, have been documented as effective in the mouse model, the next step is to investigate their effectiveness when they are both present in the same system. There has been recent evidence suggesting that there is *in vivo* compatibility of WR–2721 and misonidazole (Sodicoff *et al.*, 1979; Yuhas *et al.*, 1977). Here, we have examined the modification of the ORD syndrome due to combined WR–2721 and misonidazole.

MATERIALS AND METHODS

All experiments were performed using isogeneic female Balb/c mice of ages seven to nine weeks. The mice were housed six per cage and fed Mouse Chow #5015 and water *ad libitum*.

Irradiations were performed using a Picker V–9 ^{60}Co teletherapy unit. Dose rates were measured in air employing a Victoreen Model 621 ionization chamber directly calibrated at the National Bureau of Standards. The mice were placed in a specially constructed jig to eliminate head movement during irradiation. Only the head and neck region was exposed to the direct beam while the remainder of the body was shielded with lead blocks. The dose rate was 150 cGy (rad) per minute and irradiation times ranged from 8 to 30 min.

WR–2721 and misonidazole were dissolved in distilled water and isotonic saline respectively, immediately before injection. Mice receiving both drugs were injected simultaneously. All injections were performed intraperitoneally 30 min before irradiation.

Statistical analysis of LD_{50} curves was performed by the log-probability method (Litchfield and Wilcoxon, 1949).

RESULTS

As a result of the ORD syndrome either in the presence or absence of radiomodifying drugs, death of the mouse occurs in 10 ± 1 days. Death is due to diffuse mucosal damage in the oral cavity which ultimately leads to nutritional insufficiency. The upper curve in Fig. 1 represents the dose response relation for the ORD syndrome with single doses in drug-free mice and gives an $LD_{50/10}$ of 1650 ± 75 cGy (rad). Mice treated with 1000 mg/kg misonidazole 30 min before irradiation also demonstrate an ORD syndrome $LD_{50/10}$ of 1650 ± 75 cGy (rad) as seen in the lower curve of Fig. 1.

In order to investigate the use of combined WR–2721 and misonidazole, toxicity studies were performed. Lethal doses of the drug combinations resulted in death within 72 hours. However, the mice were observed for a total of 30 days and the results were scored as the toxic $LD_{50/30}$. Figure 2 is the isobologram analysis of the combination of the two

---

*Supported in part by research grant from the National Cancer Institute PO1–CA–17786 and RO1–CA–13849.

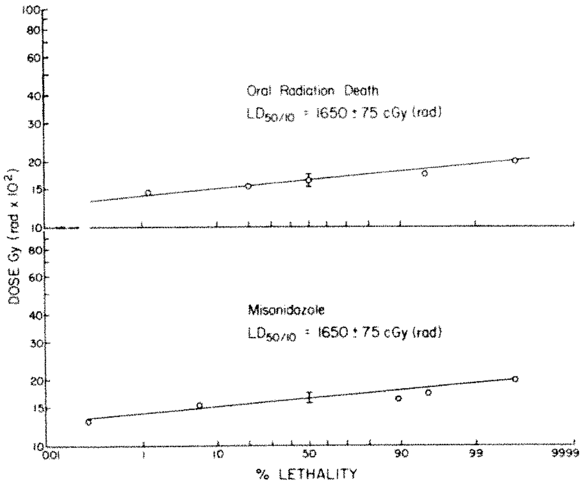


Fig. 1.

The upper curve represents the dose-response relation for the ORD syndrome with single doses. The lower curve is the equivalent response when misonidazole (1000 mg/kg) was given thirty minutes before irradiation.

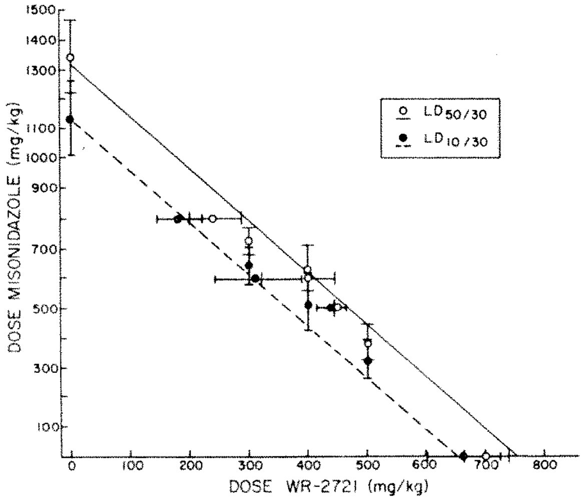


Fig. 2.

Isobologram of drug toxicity demonstrating the additive toxicity of WR-2721 and misonidazole. The upper curve is the $LD_{50/30}$ response and the lower curve is the $LD_{10/30}$ response.

drugs. These curves were obtained by titrating the toxicity levels of one drug against the other and vice versa. The endpoint for the upper curve is the toxic $LD_{50/30}$ ($r=0.994$) and that of the lower curve is the toxic $LD_{10/30}$ ($r=0.991$). These curves are linear along the unique line defining the additive toxicity of the two drugs.

The protective effect of WR-2721 on the ORD syndrome $LD_{50/10}$ is seen in Fig. 3. The dose

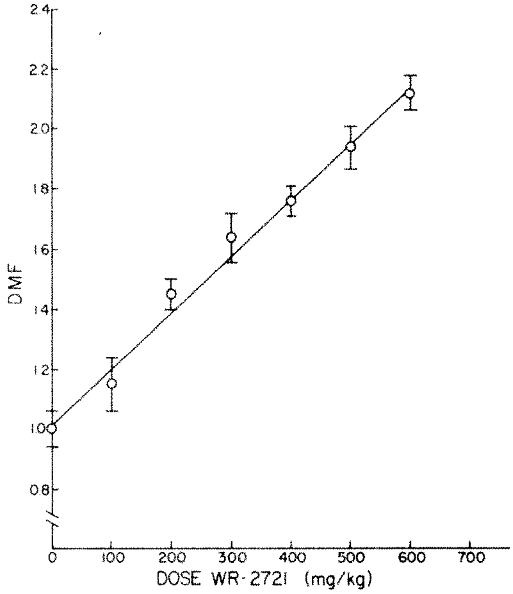


Fig. 3.

DMF as a function of dose of WR-2721 using the ORD syndrome endpoint.

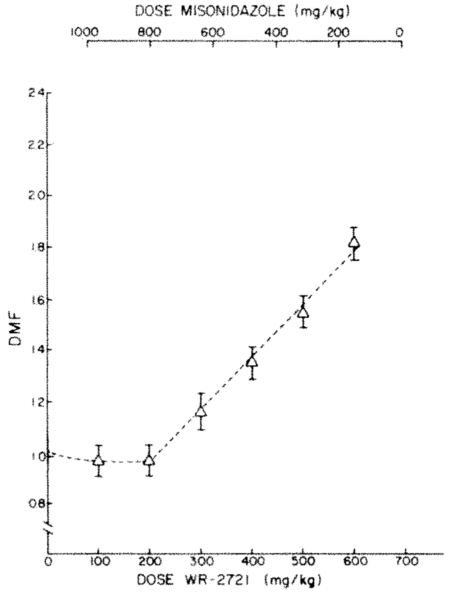


Fig. 4.

DMF as a function of combined WR-2721 and misonidazole using the ORD syndrome endpoint. Drug-dose combinations are ascertained by a vertical line connecting the upper and lower abscissas.

modification factor (DMF) for the $LD_{50/10}$ endpoint is plotted against dose of WR–2721 administered 30 min before irradiation with a single dose. This curve was produced by performing a series of $LD_{50/10}$ experiments with doses of WR–2721 ranging from 100 mg/kg to 600 mg/kg in steps of 100 mg/kg. In this system a linear response is observed throughout the range of doses tested ($r=0.994$).

The effect of both WR–2721 and misonidazole on the ORD syndrome is seen in Fig. 4. Here the DMF for the ORD $LD_{50/10}$ endpoint is plotted against the doses of the combinations of the two drugs obtained from the toxic $LD_{10/30}$ curve in Fig. 2. Since the combinations of the two drugs are chosen from the linear response of their combined effects, the doses of the two drugs used can be plotted on the same axis. Therefore, the dose of each drug is ascertained by a vertical line connecting the upper (misonidazole) abscissa and the lower (WR–2721) abscissa. At low doses of WR–2721 and high doses of misonidazole the $LD_{50/10}$ is not significantly different from the $LD_{50/10}$ of drug-free animals as seen in Fig. 1. However, after an apparent threshold at 200 mg/kg of WR–2721 and 800 mg/kg of misonidazole, the response is linear ($r=0.997$) and parallels the curve in Fig. 3.

CONCLUSIONS

The ORD syndrome provides an excellent endpoint for the study of normal tissues. Animal death, due to diffuse mucosal damage in the oral cavity, is normally distributed around day ten. Sensitization of normal tissue does not occur at the dose level of 1000 mg/kg of misonidazole and we have assumed that sensitization would not occur at lower doses of this drug.

Yuhas (1970) has demonstrated that the dose-response protective effect of WR–2721 is a power function with a plateau at high doses (500 mg/kg). In our system, the response is linear up to a dose of 600 mg/kg WR–2721 and no plateau is observed.

Studies on the combination of WR–2721 and misonidazole are limited. However, other investigators (Yuhas *et al.*, 1977) have performed toxicity studies of the two drugs and conclude that additive toxicity does not occur. Our studies demonstrate that definite additive toxicity (Steel and Peckham, 1979) occurs when the two drugs are used in combination. This apparent difference may be due to the time sequence in which the drugs were administered. In our series the drugs were administered simultaneously whereas Yuhas *et al.* (1977) injected misonidazole 30 min before injecting WR–2721.

Whether the simultaneous injection of the two drugs and the subsequent additive toxicity is by the mechanism of independent action at different sites or combined effects at a single site is unresolved.

Our studies also indicate that the radioprotective ability of WR–2721 is reduced when used in combination with misonidazole. The exact mechanism of action of WR–2721 is unknown. It has been established that WR–2721 produces a reduction in peripheral oxygen tension in air-breathing mice (Yuhas *et al.*, 1973). This suggests that the mechanism of action is the production of cellular hypoxia. It has also been demonstrated that WR–2721 must enter the cell in order to produce its protective effect (Yuhas *et al.*, 1980). Our data indicate that at low doses of WR–2721 and high doses of the hypoxic cell sensitizer, misonidazole, the protective ability of WR–2721 is diminished. If the above mechanism of action of WR–2721 is correct, then the response that we have demonstrated may be due to the sensitization by misonidazole of the hypoxic cells produced by WR–2721.

From our data we conclude that: 1) WR–2721 and misonidazole produce additive toxicity when injected simultaneously; 2) the combination can provide an overall protective response to the ORD syndrome; and 3) the combination may be potentially useful for the treatment of cancers of the oral cavity.

REFERENCES

DENEKAMP, J., and HARRIS, S. R., 1975. Tests of two electron-affinic radiosensitizers in vivo using regrowth of an experimental carcinoma. *Radiation Research, 61*, 191–203.

GRIGSBY, P.W., and MARUYAMA, Y., 1980. An experimental oral radiation model for the study of head and neck tumors using combined radiosensitization and radioprotection. In *Radiation Sensitizers: Their Use in the Clinical Management of Cancer*. Ed. by L. W. Brady. (Cancer Management Series) (Masson, New York), 506–509.

LITCHFIELD, J. T., and WILCOXON, F., 1949. A simplified method of evaluating dose-effect experiments. *Journal of Pharmacology and Experimental Therapeutics, 96*, 99–113.

QUASTLER, H., AUSTIN, M. K., and MILLER, M., 1956. Oral radiation death. *Radiation Research, 5*, 338–353.

SODICOFF, M., CONGER, A. D., PRATT, N. E., SINESI, M., and TREPPER, P., 1979. Chemoradioprotection of the rat parotid gland by combined use of WR–2721 and Ro–07–0582. *Radiation Research, 80*, 348–353.

SODICOFF, M., CONGER, A. D., TREPPER, P., and PRATT, N. E., 1978. Short-term radioprotective effects of WR–2721 on the rat parotid glands. *Radiation Research, 75*, 317–326.

STEEL, G. G., and PECKHAM, M. J., 1979. Exploitable mechanisms in combined radiotherapy–chemotherapy: the concept of additivity. *International Journal of Radiation Oncology, Biology and Physics, 5*, 85–91.

UTLEY, J. F., KING, R., and GIANSANTI, J. S., 1978. Radioprotection of oral cavity structures by WR–2721. *International Journal of Radiation Oncology, Biology and Physics, 4*, 643–647.

YUHAS, J. M., 1970. Biological factors affecting the radioprotective efficiency of S–2–(3–aminopropylamino) ethylphosphorothioic acid (WR-2721). $LD_{50/30}$ doses. *Radiation Research*, *44*, 621–628.

YUHAS, J. M., PROCTOR, J. O., and SMITH, L. H., 1973. Some pharmacologic effects of WR-2721: their role in toxicity and radioprotection. *Radiation Research*, *54*, 222–233.

YUHAS, J. M., SPELLMAN, J. M., and CULO, F., 1980. The role of WR-2721 in radiotherapy and/or chemotherapy. *Cancer Clinical Trials*, *3*, 211–216.

YUHAS, J. M., YURCONIC, M., KLIGERMAN, M. M., WEST, G., and PETERSON, D. F., 1977. Combined use of radioprotective and radiosensitizing drugs in experimental radiotherapy. *Radiation Research*, *70*, 433–443.

Book reviews

Radiation Protection Optimization—Present Experience and Methods. Ed. by A. Oudiz, G. Uzzan, H. Ebert and H. Eriskat, pp. 322, 1981 (Pergamon Press, Oxford/New York/Toronto), $50.00.
ISBN 0-08-027291-6

This volume contains the papers and the formal discussions given at a meeting in October 1979 under the aegis of the Commission of the European Communities in Luxemburg, when some three dozen nuclear energy and radiation protection experts met to discuss "optimization". The principle is that radiation exposures of the public and workers should be as low as is reasonably achievable (ALARA), economic and social factors being taken into account, but the practical application of this principle bristles with problems—conceptual, philosophical and economic. There was much discussion on the monetary value of a man-rem (or 0.01 man-Sievert, if you prefer) and what detriments from radiation should be incorporated into the calculation. Values of the order £100 per man-rem were suggested but were not agreed by all, and a speaker from NRPB argued that this was in any case an inherently variable parameter.

Almost all the discussion centred on ALARA in nuclear energy, principally in respect of population doses, but there was also discussion of its relevance to the radiation received by radiation workers. The only reference to optimization in medicine came in a round-table discussion chaired by Sir Edward Pochin. It was suggested that it would not be too expensive to eliminate superfluous man-rem doses in medicine, and others suggested that a meeting to discuss this would be fruitful. The Chairman mentioned that in Japan, where cancer of the stomach is common, it can be detected in early and treatable stages by radiology, but an optimization calculation shows that population surveys of people under the age of 30 would probably detect fewer treatable cases than the number of cases of cancer likely to be caused by the radiation. He pointed out that, on a broader scale, optimization in medicine would cost a great deal of money on new equipment and better training of personnel, and doubted whether man-rems saved would be worth the costs involved. This reviewer would only comment that a detailed study might well show Sir Edward to be right, but it should be carried out anyway.

This volume is in general well presented, but it is obvious that much of the discussion, at least, has been transcribed from tape by someone not well-versed in colloquial English. The result is that there are many obscure sentences that suddenly make sense when one word is changed for another which sounds similar. It also suffers from being a collection of papers, some of which represent the exercising of pet hobby horses, leaving the reader with the feeling that the subject has not been uniformly covered. It is, however, a welcome and worthwhile collection of papers on a subject to which increasing attention needs to be paid.

S. B. OSBORN.

Environmental Health Criteria 14: Ultraviolet Radiation, pp. 110, 1979 (World Health Organization, Geneva; Henry Kimpton, London), £4.
ISBN 92-4-154074-5.

This book presents the report of an international WHO task group which met in Geneva in 1978 to review and revise the document containing the third draft of criteria and to make an evaluation of the health risks from exposure to ultra-violet radiation. It is published under the joint sponsorship of the United Nations Environment Programme, the World Health Organization and the International Radiation Protection Association.

The document, which is in eight sections, begins with a summary and some recommendations for further studies, these being drawn from areas where the committee was conscious of a lack of reliable data on which to base firm conclusions. The middle sections cover the properties and measurement of UVR, summaries of the biological effects on unicellular organisms and cultured cells, effects on vertebrate animals and the effects on man. The remaining sections deal with evaluation of the health risks for man and guide lines for health protection, and a bibliography of publications cited in the text.

The summaries are well written and cover a very wide range of topics, inevitably at times rather superficially but adequate for the purposes of radiation safety.

For those looking for stringent mathematical evaluations of dosimetry and well-defined permissible levels like those which exist for ionizing radiations, the document will be disappointing. However, there are many complexities in the problems for UVR which do not occur with ionizing radiation. With sunlight as the primary source, one starts with inescapable exposure of the whole population, with confounding factors of locational, meteorological, and ethnic/genetic global variations. There is also the need to balance the beneficial and cosmetic effects against the harmful, carcinogenic effects.

Add to this the difficulties of monitoring personal exposure and structuring and enforcing the necessary legislation to control it within safe limits (maximum permissible sunbathing limits would not go down too well with the average holidaymaker in a British summer!) and one is faced with a formidable task.

Overall, the document provides a very fair appraisal of these problems and some reasonable recommendations, given the data currently available.

J. R. K. SAVAGE.

Repair of sublethal and potentially lethal damage in lung cells using an *in vitro* colony method

By P. J. Deschavanne, D.Sc., Marcelle Guichard, Ph.D. and E.-P. Malaise, M.D., Ph.D.

Institut de Radiobiologie Clinique, Institut Gustave-Roussy, 94805 Villejuif, France

(*Received August 1980 and in revised form May 1981*)

ABSTRACT

The repair of radiation damage has been measured in mouse lung using an *in vitro* colony assay. Following a single dose of 10.5 Gy delivered to the lung *in vivo*, we observed, six hours after irradiation, an increase of the fraction of surviving cells, which did not change further between six and 24 hours (repair of potentially lethal damage). A similar observation was made using a split-dose method (repair of sublethal damage). The extent of radiation repair is comparable with that of other rodent cells irradiated *in vivo*. The significance of these results is discussed in relation to the late effects observed following irradiation of lung tissue.

Long experience in radiotherapy has shown that fractionated irradiation generally leads to an increased therapeutic ratio due, among other reasons, to better protection of normal tissues relative to tumours. This principle, established primarily with the skin and the mucosa of the upper respiratory–digestive tract, is also valid for the lung but to a lesser extent. Nevertheless, in terms of the mean tolerance dose, the lung remains one of the most radiosensitive tissues, even with a fractionated regimen (Rubin and Casarett, 1972).

Using an *in-vitro* colony assay, we have shown previously that the inherent radiosensitivity of murine lung cells is comparable to that of cells from other tissues (Guichard *et al.*, 1980). Thus, it does not appear that the intrinsic radiosensitivity of lung cells, as determined by short-term measurements of survival curves, can explain lesions occurring later in lungs receiving 25 Gy fractionated over many sessions.

The aim of this work is to extend previous findings by determining the possible influence of another factor determining radiosensitivity, which occurs between sessions of fractionated irradiation, viz repair of radiation damage.

METHODS AND MATERIALS

Mice

We used three to five week old female heterozygote nu/+ mice maintained in a sterile environment.

Lung cell culture

The culture method has been described elsewhere (Guichard *et al.*, 1980). Briefly, animals were killed by cervical dislocation and were submerged in a solution of 1% cetrimonium bromide in alcohol for seven to ten minutes. The lungs were removed aseptically and minced with scissors. Tissue fragments were immersed in 40 ml of calcium-free 0.25% crystallized trypsin solution for 25 min at 37°C with continuous agitation. Trypsinization was stopped by adding 8 ml of calf serum. After centrifugation, the supernatant was discarded and the cells were resuspended in Eagle's minimum essential medium (MEM Earle's salt). A suspension of single cells was obtained by passing the cells through a stainless steel filter with 18 μm pore diameter. The cells were counted and seeded in plastic flasks containing HF 19 feeder cells (4×10^3 cells/cm^2 which had received 30 Gy) and MEM supplemented with 20% fetal calf serum, 50 mg/litre kanamycin and 15 mg/litre gentamycin. The flasks were then placed in a CO_2 incubator at 37°C. The culture medium was changed six to seven days after plating; after ten to 12 days of culture, colonies were fixed, stained and counted with an inverted microscope.

Irradiation

Mice were irradiated *in toto* with ^{137}Cs γ rays at an average dose rate of 1.6 Gy/min. The average dose rate for feeder cells was 8.0 Gy/min. The precision of the dose was about ±2% in the former case and ±5% in the latter.

RESULTS

The average plating efficiency of lung cells under our experimental conditions was 8.2%. With this culture technique applied to a tissue dissected directly from the animal, we obtained colonies exhibiting mainly two morphological types, those composed of fibroblast-like cells and those composed of epithelial-like cells. These two types of colony were encountered in all our experiments. Controls yielded 43% fibroblast-like and 51% epithelial-like colonies. It was previously shown that the two types of colony could not be distinguished by histochemical methods (Guichard *et al.*, 1980). The biological significance of these morphologies thus remains to be elucidated and so it appeared preferable to measure radiosensitivity independently of cell morphology.

Repair of radiation damage was studied in two ways. The repair of potentially lethal damage (PLD) was assessed by excising the lung and plating cells after different post-irradiation time intervals. Survival curves were generated for cells plated from lungs excised immediately or 24 hours after irradiation (Fig. 1). Parameters, calculated by linear regression on the logarithms of survivals, are respectively $n=3.9$, $D_0=1.58$ Gy, and $n=2.5$, $D_0=2.52$ Gy. The kinetics of repair was then studied by determining the surviving fraction after a dose of 10.5 Gy delivered *in vivo* followed by plating of cells at varying intervals between zero and 24 hours after irradiation. We observed a significant increase between zero and six hours ($P < 0.05$), with no further increase between six and 24 hours. The surviving fraction at 24 hours was six times higher than at time zero (Fig. 2).

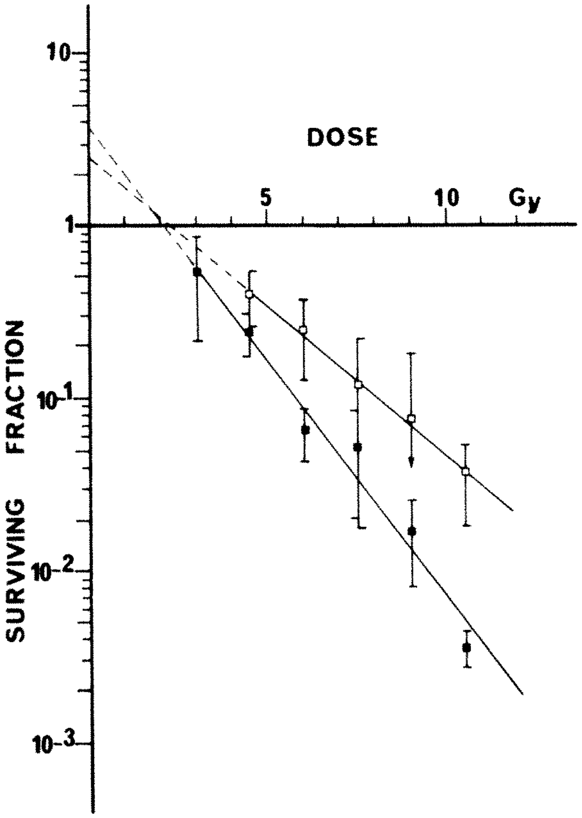


FIG. 1.

Survival curves of lung cells obtained upon excision of the lung immediately post-irradiation (■——■) and 24 h post-irradiation (□——□). The error bars represents the 95% confidence intervals (t-test).

Secondly, we used the split-dose method (Elkind and Sutton, 1960) for studying the repair of sublethal damage with time intervals from zero to 24 hours, separating two doses of 5.25 Gy. In this case, cells were plated as soon as possible after the second dose. Of course, we measured both repair of PLD occurring after the first dose and the repair of sublethal damage occurring between the two doses. The surviving fraction in split-dose experiments increased significantly for intervals up to three hours, and there was no further change up to 24 hours. The surviving fraction at 24 hours was 15 times higher than at time zero (Fig. 3).

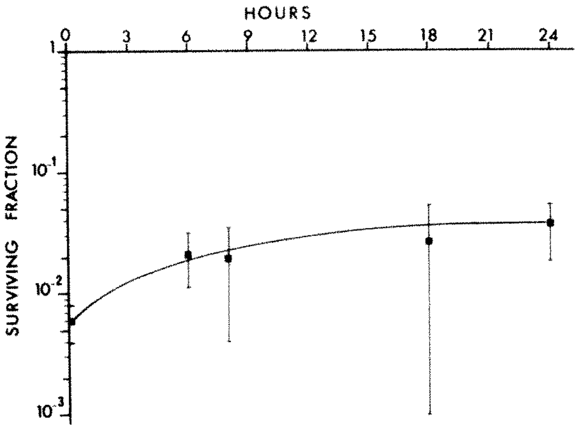


FIG. 2.

Repair of potentially lethal damage after a dose of 10.5 Gy as a function of the time interval between irradiation and killing of the animal. The error bars represents the 95% confidence intervals (t-test). Each point represents the mean value for 17, 19, 7, 11 and 20 animals at 0, 6, 8, 18 and 24 h respectively.

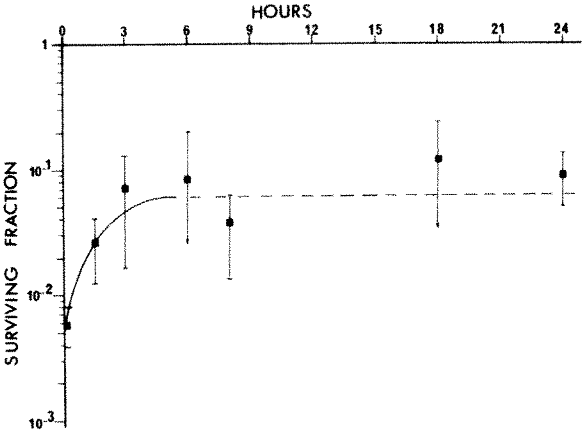


FIG. 3.

Repair of sublethal damage as a function of the time interval separating two doses of 5.25 Gy each. The error bars represents the 95% confidence intervals (t-test). Each point represents the mean value for 17, 10, 15, 12, 10, 4 and 9 animals at 0, 1.5, 3, 6, 8, 18 and 24 h respectively.

Discussion

The method used for preparing single-cell suspensions poses the problem of the representative nature of these cells; indeed, we recovered only a small proportion of lung cells (Guichard *et al.*, 1980) and the plating efficiency was about 8.2% (±1.25%, 95% confidence interval). Two different factors are probably responsible for such a PE: a relatively aggressive cell dispersion technique and the possibility that the colonies arise from stem cells which constitute only a fraction of the total cell population. Three experimental findings appear to be encouraging: plating efficiency is relatively high compared with those obtained by other authors working with different normal tissues (for survey see Deschavanne *et al.*, 1980); plating efficiency in about 15 experiments spread over a period of four years remained stable, as have the respective proportions of epithelial-like and fibroblast-like cell colonies.

Measurement of the recovered dose per fraction (D_2-D_1) was the first method used to evaluate the extent of repair occurring during fractionated irradiation of normal tissues with a low turnover rate, such as lung (Phillips, 1972). This recovered dose results from the interaction of many factors, such as radiation damage repair, redistribution and repopulation. Furthermore, since the recovered dose itself depends on the initial dose, this concept is not always well adapted for comparing the responses of different tissues to fractionated irradiation. More recently it has been proposed to measure repair of radiation damage by the uptake of ^{14}C-thymidine into the DNA of lung cells after stimulation by the antioxidant butylated hydroxytoluene (Meyer and Ullrich, 1981). Using an *in vitro* colony method, we attempted to determine the contribution of two of the factors which can occur between fractions: the repair of sublethal damage and of potentially lethal damage.

Mouse lung is a rather radiosensitive tissue, since the lethal dose (LD) 50/180 for a single dose is about 11 Gy. The recovered dose (D_2-D_1) is, however, not negligible (3.0–4.0 Gy) (Phillips and Margolis, 1972). From this point of view lung tissue is in the middle zone of Phillips' classification system (Phillips, 1972). Our results, too, show that repair of radiation damage in lung cells is not negligible. Although it is difficult to compare results obtained by different methods, it appears that the types of repair we describe can, at least partially, explain the recovered dose determined by Phillips and Margolis (1972). Furthermore, using the labelled thymidine uptake method, Meyer and Ullrich (1981) also demonstrated an increased proportion of proliferating cells in animals tested 24 hours after irradiation.

Using the split-dose method, we observed an increase of surviving cells, probably explained by the cumulative effect of the repair of sublethal damage and of potentially lethal damage after the first dose of 5.25 Gy. Under these conditions, we would expect a survival level of the order of 3.5×10^{-2} after two doses of 5.25 Gy each, separated by 24 hours, calculated from the fitted curve using the formula:

$$S=S(5.25\text{ Gy, }24\text{ h})\times S(5.25\text{ Gy, }0\text{ h}).$$

The observed survival fraction was greater than that calculated, confirming that the two types of repair did indeed occur together.

The extent of repair occurring in lung cells *in vivo* can be compared with that observed in normal rodent tissues: mouse embryo (Ohnuma *et al.*, 1978), mouse kidney cells (Guichard *et al.*, 1981), rat mammary gland cells (Gould and Clifton, 1979), capillary endothelium (Reinhold and Buisman, 1975) and rat thyroid cells (Mulcahy *et al.*, 1980). The same comparison may be made with murine or rat tumours irradiated *in vivo* (Hahn *et al.*, 1974; Little *et al.*, 1973; McNally and Sheldon, 1977; Urano *et al.*, 1976; Wheeler *et al.*, 1980). The repair of potentially lethal damage may result either in a change of the slope of the survival curve (D_0) or in a modification of the shoulder, *i.e.* D_q. In most cases, however, repair of PLD decreases the slope of the curve. The two exceptions occurring in normal tissues are mammary gland and thyroid cells (Gould and Clifton, 1979; Mulcahy *et al.*, 1980). In these two cases, the results were obtained with a different method, and therefore it is difficult to exclude bias arising from a relationship between the results and the technique used. In the literature devoted to PLD repair we did not find complete survival curves before and after repair for all the cell lines investigated. We thus calculated the repair factor by dividing the fraction of cells surviving a given dose and plated after a certain delay by the surviving fraction of the same cells irradiated identically and plated immediately (Table I). The zero time survival level for these different cell lines and/or tissues was selected to be of the same order of magnitude, so that the resulting ratio could be used to compare the extent of PLD repair (Table I). With the exception of murine embryo cells, it appears that maximal PLD repair is comparable for all the tissues mentioned above.

Using a split-dose method, Field *et al.* (1976) and Field and Hornsey (1977) demonstrated a slow repair, observable over a six-week period following

TABLE I

REPAIR OF POTENTIALLY LETHAL DAMAGE FOR SOME RODENT CELLS IRRADIATED *IN VIVO*

$$\text{Repair factor} = \frac{\text{maximal surviving fraction reached with delayed plating}}{\text{surviving fraction of cells plated as soon as possible after irradiation}}$$

Tissue origin	Surviving fraction at 0 h	Repair factor*	Reference
Normal tissue			
Mouse lung	6.7×10^{-3}	6.0	This work
Rat mammary gland	10^{-3}	3.2	Gould *et al.*, 1979
Mouse kidney	4.4×10^{-3}	3.9	Guichard *et al.*, 1981
Mouse embryo	1.5×10^{-3}	20.0	Ohnuma *et al.*, 1978
Rat capillary endothelium	2×10^{-2}	4.0	Reinhold *et al.*, 1975
Rat thyroid	10^{-3}	6.5	Mulcahy *et al.*, 1980
Tumour cells			
EMT6 cells	3.6×10^{-3}	5.3	Hahn *et al.*, 1974
NCTC ascites (8 day old tumour)	—	3.8	Little *et al.*, 1973
NCTC solid tumour (> 1 cm^3)	—	3.5	Little *et al.*, 1973
MT cells	2×10^{-3}	4.2	McNally *et al.*, 1977
Nr S1 cells	2×10^{-3}	7.5	Urano *et al.*, 1976
9L	4.7×10^{-3}	10.0	Wheeler *et al.*, 1980

*The different repair factors were evaluated from figures presented in the publications.

γ-ray irradiation of mouse lung. Using either split-dose irradiation or delayed plating, we detected no significant differences between the 24 hour delayed plating surviving fraction and the six hour surviving fraction. There are two reasons for which we believe that our results and those of Field *et al.* are not contradictory. First, our observation period was shorter (24 h) than theirs. Second, the slope of the recovery curve obtained by these authors was gradual and so the increase of the surviving fraction between six and 24 hours may be included in the confidence interval of our values.

We previously showed that it is not possible to explain the high long-term radiosensitivity of the lung by the intrinsic radiosensitivity of lung cells as estimated by the survival curve (Guichard *et al.*, 1980). Indeed, the latter is comparable to those of many mammalian cells. The same argument is also valid for the repair of radiation damage, whose extent is of the same magnitude as that observed for many other tissues.

In conclusion, it seems that there is a contrast between the short-term radiosensitivity of lung cells measured *in vitro* and the long-term radiosensitivity of lung as measured by gross reactions. It is likely that these gross reactions depend on other factors, such as damage to connective or vascular tissues and/or the number and the long-term division potential of the stem cells of the pulmonary parenchyma.

ACKNOWLEDGMENTS

This research was supported in part by grant 78.5.170.2 from the Institut National de la Santé et de la Recherche Médicale and by the Ligue Nationale Contre le Cancer (Département des Hauts-de-Seine).

REFERENCES

DESCHAVANNE, P. J., GUICHARD, M. and MALAISE, E. P., 1980. Radiosensitivity of mouse kidney cells determined with an *in vitro* colony method. *International Journal of Radiation Oncology, Biology and Physics*, *6*, 1551–1557.

ELKIND, M. M. and SUTTON, H., 1960. Radiation response of mammalian cells grown in culture. I. Repair of X-ray damage in surviving Chinese hamster cells. *Radiation Research*, *13*, 556–593.

FIELD, S. B. and HORNSEY, S., 1977. Slow repair after X rays and fast neutrons. *British Journal of Radiology*, *50*, 600–601.

FIELD, S. B., HORNSEY, S. and KUTSUTANI, Y., 1976. Effects of fractionated irradiation on mouse lung and a phenomenon of slow repair. *British Journal of Radiology*, *49*, 700–707.

GOULD, M. N. and CLIFTON, K. H., 1979. Evidence for a unique *in situ* component of the repair of radiation damage. *Radiation Research*, *77*, 149–155.

GUICHARD, M., DESCHAVANNE, P. J. and MALAISE, E. P., 1980. Mouse lung cells radiosensitivity measured using an *in vitro* colony method. *International Journal of Radiation Oncology, Biology and Physics*, *6*, 441–447.

1981. Repair of sublethal and potentially lethal damage in kidney cells using an *in vitro* colony method. Submitted to the *International Journal of Radiation Biology*.

HAHN, G. M., ROCKWELL, S., KALLMAN, R. F., GORDON, L. F. and FRINDEL, E., 1974. Repair of potentially lethal damage *in vivo* in solid tumor cells after X-irradiation. *Cancer Research*, *34*, 351–354.

LITTLE, J. B., HAHN, G. M., FRINDEL, E. and TUBIANA, M., 1973. Repair of potentially lethal radiation damage *in vitro* and *in vivo*. *Radiology*, *106*, 689–694.

MCNALLY, N. J. and SHELDON, P. W., 1977. The effect of radiation on tumour growth delay, cell survival and cure of the animal using a single tumour system. *British Journal of Radiology*, *50*, 321–328.

MEYER, K. R. and ULLRICH, R. L., 1981. Effects of X rays and fission neutrons on an induced proliferative response in lung type II epithelial cells. *Radiation Research*, *85*, 380–389.

MULCAHY, R. T., GOULD, M. N. and CLIFTON, K. H., 1980. The survival of thyroid cells: *in vivo* irradiation and *in situ* repair. *Radiation Research*, *84*, 523–528.

OHNUMA, N., URANO, M., KOIKE, S. and TERASIMA, T., 1978. Repair of potentially lethal radiation damage in mouse embryo. *European Journal of Cancer*, *14*, 649–651.

PHILLIPS, T. L., 1972. Split-dose recovery in euoxic and hypoxic normal and tumor cells. *Radiology*, *105*, 127–134.

PHILLIPS, T. L. and MARGOLIS, L., 1972. Radiation pathology and the clinical response of lung and esophagus. In *Radiation effect and tolerance, normal tissue. Basic concepts in radiation pathology. Frontier of Radiation Therapy Oncology*, Ed. by J. M. Vaeth, *6* (Karger, Basel), pp. 254–273.

REINHOLD, H. S. and BUISMAN, G. H., 1975. Repair of radiation damage to capillary endothelium. *British Journal of Radiology*, *48*, 727–731.

RUBIN, P. and CASARETT, G., 1972. A direction for clinical radiation pathology: the tolerance dose. In *Radiation effect and tolerance, normal tissue. Basic concepts in radiation pathology. Frontier of Radiation Therapy Oncology*, Ed. by J. M. Vaeth, *6* (Karger,Basel), pp. 1–16.

URANO, M., NESUMI, N., ANDO, K., KOIKE, S. and OHNUMA, N., 1976. Repair of potentially lethal radiation damage in acute and chronically hypoxic tumor cells *in vivo*. *Radiology*, *118*, 447–451.

WHEELER, K. T., NORTON, K. L., DEEN, D. F. and LEITH, J. T., 1980. *In situ* recovery from potentially lethal damage after irradiation with BEVALAC accelerated carbon ions. *International Journal of Radiation Biology*, *37*, 225–229.

Book review

Natural Radiation Environment III, Vol. 1 and 2. Ed. by T. F. Gesell and W. M. Lowder, pp. 853+xiv, 882+vx, 1980 (Technical Information Center, U.S. Department of Energy, Oak Ridge, Tenn.), $39.50 (for two volumes, not available separately).
ISBN 0-87079-119-2

The proceedings of this symposium on natural radiation reproduce the 110 papers which were presented. They were grouped into the 10 topic sections summarised briefly below.

Radon in the Ground covers the work on measuring and calculating the movement of radon in soils and rocks and its emanation from them to the atmosphere. These papers present analyses of the important factors in the rate at which radon can reach the human environment.

Seismicity and Radioactivity has only two papers and these discuss the monitoring of emanation rates of radioactive gases for use in earthquake prediction. These rates are a useful predictor but only in conjunction with other information.

Radioactivity in the Atmosphere is influenced by meteorological and geological conditions. This section contains reports on these effects and on the global distribution of some of the longer-lived daughters of radon. This distribution seems also to be affected by solar activity.

Radionuclides in Marine Systems and Radionuclides in Aquatic and Terrestrial Systems covers radon and radium in the ocean and in ground waters and their movement in soils due to animals and plants. Papers on radionuclides such as strontium 90, caesium 137 and trace metals also appear in these sections.

Radionuclides in Food and Tissue contains reports on concentrations of radio-isotopes in food materials and in human tissue. One paper discusses uptake from soil by vegetation and another the presence of radium and thorium in micronodules in the thyroid of cattle.

Penetrating Radiation Measurements includes papers on cosmic-ray neutrons, measurement techniques and in particular the use of thermoluminescence to assess natural background gamma radiation.

Radiation Surveys and Population Exposure is concerned mostly with reports on levels in particular countries or in areas of unusual radiation features.

Radioactivity in the Indoor Environment concentrates on radon and thoron and their decay products inside buildings. Most papers deal with building materials as the source of radon although papers on emanation from soil and natural rock also appear.

Technologically Enhanced Natural Radioactivity is a section for studies of increased exposure to naturally occurring radiation brought about by human activity. The definition does not always include the same range of activities—for example some would wish to include high-altitude flight in an aeroplane within the terms while others would exclude it since the radiation field has not been changed (the additional exposure resulting because man puts himself in the field). The papers in this section cover the redistribution of radioactivity by uranium and phosphate mining, the coal fuel cycle and industrial discharges into rivers.

These proceedings provide a panoramic snapshot of the state of knowledge and the work in progress on the natural radiation sources in our environment as of 1978. The two volumes are not suitable for general reading because by the nature of conference papers there is a strong element of repetition and the reports are prepared by specialists for other specialists. However, using the list of paper titles as an index this publication can be treated as a source of basic data.

There are papers on regulatory aspects and on remedial measures for the reduction of radiation doses associated with natural sources, as well as papers reporting research and survey projects. This collection of papers, bound in two volumes, represents a valuable reference to anyone interested in the subject matter—it would require a major effort to assemble such a comprehensive set of papers from the literature.

J. A. REISSLAND.

1981, *British Journal of Radiology*, *54*, 978–981

Technical note

The accuracy of dimensional measurement in ultrasonic real-time scanning

By *†R. C. Chivers, *R. A. Bacon and †T. J. Bloomberg

*Physics Department, University of Surrey and †Department of Diagnostic Radiology, Royal Surrey County Hospital, Guildford, Surrey GU2 5XH

(Received March 1981)

The ease of examination with real-time ultrasonic scanners, together with the provision of calipers, combine to make dimensional measurement of anatomical or pathological features an attractive index, that should ideally be independent of the operator. The traditional areas of application of dimensional measurements are obstetrics (which have been reviewed by Chivers and Dudley, 1980) and ophthalmology (Thijssen, 1973), although serial measurements on the growth of tumours and measurement of abscesses, cysts or necrotic regions (Dale *et al.*, 1980) are also of potential importance. The observations in this technical note are directed at the accuracy of the measurements made, and thus to the reliance that may be placed upon them. The discussion will be primarily concerned with situations in which the region to be measured has a relatively uniform echogenicity which is in marked contrast to its surroundings. The obvious example of this is a cystic or necrotic region, although a soft-tissue mass in a fluid-filled region would present related problems. For reasons which will become clear, the discussion may be less appropriate for very strongly reflecting structures such as large gall-stones or fetal skulls.

A CLINICAL CASE

Our attention was focused on the problem by a case of a renal cyst, illustrated in Fig. 1. Examination with a 2.4 MHz linear array revealed an almost circular cross section to the cyst, an appearance that was maintained when a second section was taken perpendicular to the first. From the caliper measurements, assuming a spherical volume, the volume of the cyst was estimated as approximately 92 ml (taking a mean diameter $d=\frac{1}{3}(58+2\times 55)$). The difference between spherical and spheroidal assumptions for the shape in the calculation of the volume was of the order of 0.1%, so the main errors to be expected would derive from caliper accuracy (± 1 mm), *i.e.* $\sim 6\%$, and the judgment of the operator on the limits

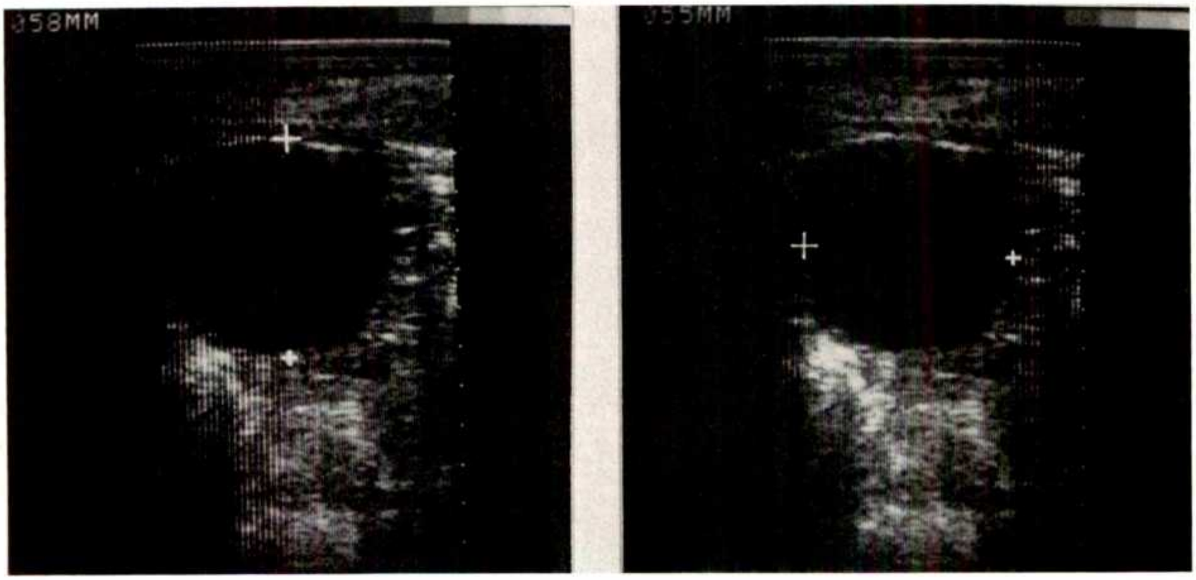


FIG. 1.

Caliper measurement of a cyst on a real-time linear array at 5 MHz.

of the cyst. On aspiration, the cyst gave 120 ml of fluid. For a discussion of the potential sources of error, it is relevant to distinguish (Fig. 2) between measurements made along the beam (longitudinally, x direction) and those made perpendicular to the beam (laterally, y direction). The error of measurement Δr in any other direction at an arbitrary angle θ to the y axis can be related to those in the x and y directions (Δx, Δy) by:

$$\Delta r = \sin\theta\Delta x + \cos\theta\Delta y \quad . \quad . \quad . \quad (1)$$

in which it is noted that the absolute errors are used rather than percentage errors.

ACCURACY OF MEASUREMENTS

Longitudinal measurement

The precision of caliper measurements varies a little from machine to machine, but measurement to within ±1 mm should prove possible on most machines. Dale *et al.* (1980) working at 3.5 MHz quote ±0.3 mm, although they do not appear to give any information as to the origin of this figure. They point out, as is generally appreciated in measurements of biparietal diameter, that the appropriate measurement is from the first echo of any front wall reflection to the first echo of the rear wall reflection, *i.e.* including the thickness of the front wall echo, which they report to vary between 1.1±0.2 mm and 0.4±0.2 mm and which varies with the settings of the brightness and gain controls. In addition these authors tabulate the results of longitudinal echographic measurements on fixed breast cysts, compared with measurements taken on subsequent sectioning. Their results are presented graphically in Fig. 3. The solid line represents the ideal, *i.e.* echographic and sectioned measurements equal. The dotted line represents the line of regression of the echographically determined value (e) on the actual value (a). The line has equation

$$e = 0.95a - 0.64 \quad . \quad . \quad . \quad . \quad (2)$$

if the two ringed points are excluded. Inclusion of these points yields:

$$e = 0.94a - 0.91 \quad . \quad . \quad . \quad . \quad (3)$$

The implication of equation (3), albeit derived from a small sample (8), is that there is a consistent underestimate of the size measured by the ultrasonogram. This underestimate has two components—a constant (absolute) underestimate of 0.64 mm and a percentage underestimate of the order of 5%. The most obvious mechanism for the latter is a difference between the ultrasonic velocity in the cyst liquid and the calibration velocity of the machine used. A higher calibration velocity would lead to an overestimate of the size. Machine velocities certainly vary by such an amount: 1540 m/s and 1600 m/s (a difference of 4%) tend to be standard for biparietal diameter measurements. The velocity variation of normal breast tissue (*e.g.* Goss *et al.*, 1978) also seems to be of the same order of magnitude, although no data on cystic fluid appear in this tabulation, and the effects of fixing do not appear to have been investigated.

The origin of the constant error is most likely to derive from the technique of measurement, and comparison of equations (2) and (3) show that it is quite sensitive to the inclusion of the two ringed

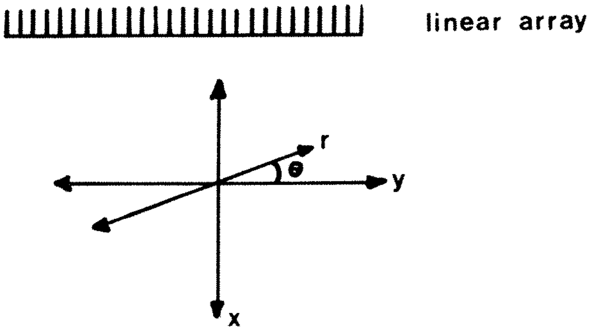


FIG. 2.

The (two-dimensional) co-ordinates. x and y are rectangular Cartesian co-ordinates, respectively perpendicular and parallel to the linear array, while r,θ are the corresponding polar co-ordinates (θ being taken from the y direction).

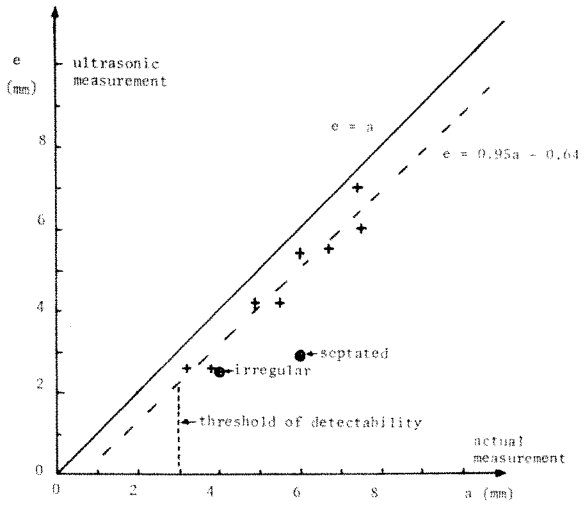
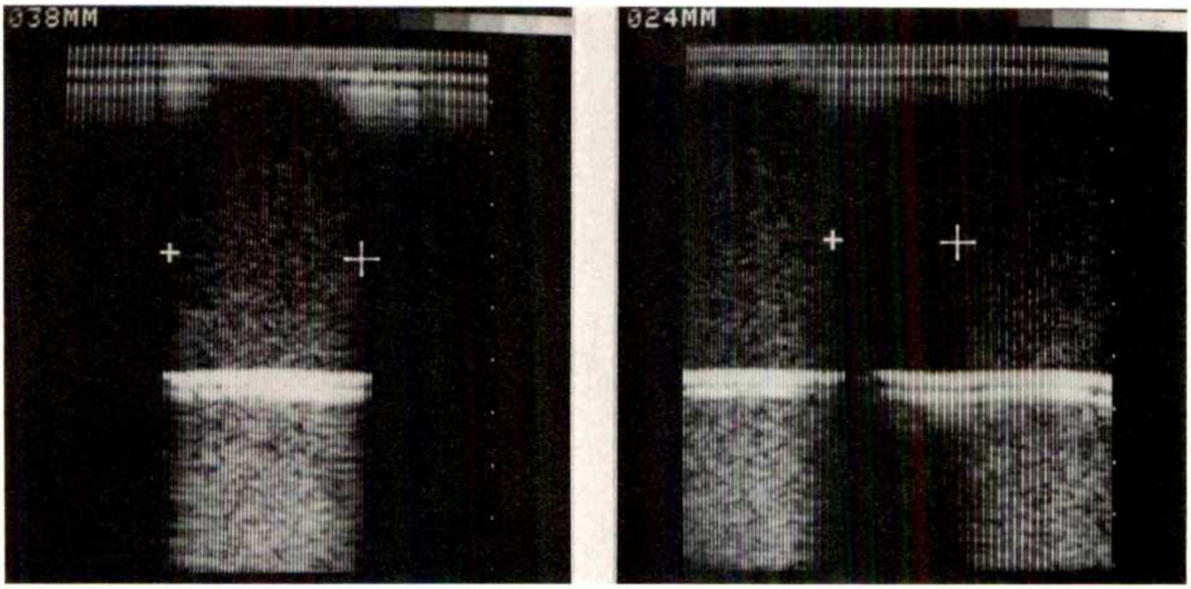


FIG. 3.

Graphical representation of the data of Dale *et al.* (1980) of the actual longitudinal cyst dimension (a) against ultrasonic measurement (e).



A FIG. 4. B

Linear scans of tissue models at 2.5 MHz: (A) a single block of scattering material; (B) a single echo-free zone. In each case the central block was 3 cm across. The caliper measurements are shown on the display.

points. The overall conclusion is that the total errors involved, which range from about 25% for the smallest detectable diameter of 3 mm to 13% for a diameter of 7.5 mm, are quite large for laboratory experiments and may be amenable to reduction. It is difficult to predict the accuracy that may be expected *in vivo* due to internal movement, etc. The figure of 5% due to velocity variation may prove to be a fundamental limit to linear measurement, which if it were also applicable to lateral measurement would indicate a limiting accuracy of 10% for measurements of area and 15% for volume. However, this is inadequate to explain the original clinical observation.

Lateral measurement

The accuracy of lateral measurement with real-time scanners depends to a large extent on their mode of operation. With linear-array scanners, the calipers may, in principle, be calibrated in a manner which is independent of the calibration velocity of the machine, being derived directly from the probe dimensions. With rotating mechanically-scanned devices and phased arrays the calibration velocity of the machine has to be involved. Typical results from some experiments using a real-time linear-array scanner at 2.5 MHz are shown in Fig. 4.

In each case the test object consisted of three tissue models (glass spheres suspended in silicone rubber) with parallel sides that produced airtight seals under slight hand pressure. In Fig.4A the two outer blocks contained no scatterers, while in Fig. 4B the centre block contained no scatterers. In each case the centre block had a thickness of 30±0.5 mm. The calipers were adjusted to measure the apparent width of the block at 2.4 MHz with the results shown, namely that the width of an isolated block of scattering material was overestimated and the width of an echo free zone underestimated by about 25%. An explanation of these results may be suggested in terms of a relatively poor lateral resolution for the scanner, which would tend to accentuate the lateral extent of scattering regions. This is consistent with the clinical case report presented. While further investigation of these easily reproducible phenomena is in progress, they have important implications for dimensional measurement with linear-array real-time scanners.

CONCLUSION

Using the figures mentioned above of 5% for the accuracy of longitudinal measurement and 25% for the accuracy of the lateral measurement, it may be implied that linear measurements may vary between these extremes, that area measurements would have an accuracy of about 30% and volume measurements of the order of 55%. These are certainly extreme cases which are based on existing observations and emphasize both the caution needed in interpreting dimensional data from real-time scanners and the need for systematic evaluation of the methods used in particular diagnostic situations.

The results presented may be moderated in practice by several factors: the differential echogenicity of the tissues on each side of the boundary, the shape of the boundary, the method of real-time scanning (*i.e.* mechanical "spinner" or phased-array devices). In addition there are the intrinsic problems of accuracy when calculations are based on sampled measurements with the assumption of geometrical regularity, and of identifying the bounds of amorphous tissue masses. The clinical example quoted gave an error of only about 25% for a volume measurement, which suggests that the figures derived from the model experiments were unduly pessimistic. However, the relatively poor lateral discrimination of linear arrays (which should not usually affect measurements of biparietal diameter) may severely prejudice dimensional measurements.

The principle of using linear regression analysis on laboratory specimens to distinguish errors of calibration from those of technique has application in a number of areas, including obstetrics.

ACKNOWLEDGMENTS

The authors wish to thank Senior Radiographer Mrs. S. Godern for her assistance, and gratefully acknowledge support from the Medical Research Council who provided the scanner and the DHSS for funding the model development.

REFERENCES

CHIVERS, R. C. and DUDLEY, H. J. W., 1980. The use of an image analyser for dimensional quantification in ultrasonic images, *Archives of Acoustics* (Warsaw), *5*, 169–180.

DALE, G., GAIRARD, B. and GROS, D., 1980. Numerical analysis of breast echotomograms. In *Investigative Ultrasonology. 1. Technical Advances.* Ed. by C. R. Hill and C. Alvisi (Pitman Medical, London), pp.33–42.

GOSS, S. A., JOHNSTON, R. L. and DUNN, F., 1978. Comprehensive compilation of empirical ultrasonic properties of mammalian tissues. *Journal of the Acoustical Society of America*, *64*, 423–457.

THIJSSEN, J., 1973. Echo-ophthalmology: physical principles and diagnostic value. In *Photography, electro-ophthalmology and echo ophthalmology in ophthalmic diagnosis.* Ed. by H. E. Henkes (Junk, The Hague), pp. 217–281.

Book review

Ultrasonic Tissue Characterization. Clinical Achievements and Technological Potentials. Ed. by J. M. Thijssen, pp.xv+292, 208 Figs., 15 Tables, 1980 (Stafleu, Amsterdam), Dutch Florins 90.00.
ISBN 90-6016-395-8

In November 1979 a workshop consisting of invited clinicians of many disciplines interested in ultrasound, a group of medical physicists and technologists together with a few engineers was held at the University of Nijmegen, the Netherlands, with the aim of discussing the state of the art in all aspects of ultrasonic tissue characterization. The 28 participants were drawn from seven European countries including the United Kingdom and Ireland. The book consists of condensations of the lectures given at the workshop. They are divided into three sections which are the clinical applications of ultrasound, the physics of the interaction of ultrasound with biological tissue and the mathematical techniques of ultrasonic signal analysis with an additional lecture on instrumentation and standardization. A survey paper preceded each of the first two sections. There are 13 papers in the section on clinical applications starting with the same review article on tissue characterization activities in ultrasound by Professor H. G. Trier (Bonn) followed by papers on tissue characterization in the breast (two papers), gynaecology, eye and orbit, liver, thyroid, gastro-enterology, heart, and also papers on the ultrasonic assessment of the thyroid, pancreatic ultrasound, the value of ultrasound in urology and echography of the mediastinum. These papers are extraordinarily informative in spite of their condensation. The next section on the physics of interaction of ultrasound with biological tissues commences with an excellent and comprehensive review article by Dr. J. M. Thijssen on the physics and technology of ultrasonography. Then come papers on the biomedical applications of acoustic microscopy, attenuation principles and measurement in tissue characterization, the principle, applicability and results of "impediography", the interference effects in the backscattered signals from human tumours, backscattering-frequency effects and finally spectrum analysis. The next section is on ultrasonic signal analysis covering A-mode video signals, A-mode RF-signal analysis, "optimal" inverse filtering and matched filtering and their relations to *in-vivo* echographic tissue differentiation, texture analysis of ultrasonic signals in the investigation of liver disease, synthetic focusing methods for ultrasonic pulse-echo systems, the application of pattern recognition of ultrasonic sectional pictures of the prostate (B-mode analysis) and analysis of soft tissue movements. After the last section is a final paper on instrumentation and standardization. All these papers in Sections 2 and 3 and the final paper make fascinating reading though they present problems of comprehension to those who are not dedicated medical physicists and mathematicians. However, none of the methods of tissue characterization described has at the present time any routine application in clinical practice though some show considerable promise. Those who have described their research in this book are to be encouraged to persist in trying to reach their goal but in the meantime those providing an ultrasonic service to patients will have to continue to rely on the presently accepted subjective criteria for diagnosis.

This book is unlikely to find a place in hospital radiodiagnostic departmental libraries, but it should be available from some more central library to those who have a need to refer to it.

F. G. M. ROSS.

1981, *British Journal of Radiology*, *54*, 982–986

Case reports

Hippel-Lindau syndrome in identical twins

By D. P. Wesolowski, M.D., R. A. Ellwood, M.D., R. E. Schwab, M.D. and J. Farah, M.D.

Department of Diagnostic Radiology, William Beaumont Hospital, Royal Oak, Michigan 48072

(*Received April 1981*)

Hippel-Lindau Syndrome (HLS) is a heritable disease complex with autosomal dominant transmission with variable penetrance and delayed expression (Christoferson *et al.*, 1961). The syndrome is characterized by retinal angiomas, CNS haemangioblastomas and cysts or solid tumours in the visceral organs, sympathetic chain, epididymis, lung and bone. Occasionally the syndrome is associated with hypertension, polycythaemia, diabetes mellitus, skin naevi and café-au-lait spots. The various expressions of the syndrome have been well described in several reports (Lee *et al.*, 1977). The necessity of a careful multidisciplinary approach to diagnosis and management is stressed.

Several large families with HLS have been studied (Christoferson *et al.*, 1961; Melmon and Rosen, 1964; Fill *et al.*, 1979; Lee *et al.*, 1977) and at least two included sets of twins who were apparently uninvolved by the disease (Richards *et al.*, 1975; Horton *et al.*, 1976). To our knowledge, this is the first report of HLS affecting identical twins and it illustrates some interesting aspects of the syndrome.

Case Reports

Case 1: Twin "A"

This 27-year-old white male complained of a two-month history of increasingly severe occipital headaches occasionally associated with unsteadiness, blurred vision and "amplification and dampening" of a constant sound source. Medication was prescribed without relief. Contrast-enhanced computed tomography (CECT) of the head revealed multiple cysts in the right cerebellar hemisphere, one containing a mural nodule; distortion and displacement of the fourth ventricle; and moderate hydrocephalus (Fig. 1A, B). On admission to hospital, the patient stated that the headaches were increasing in severity and frequency and was otherwise asymptomatic. Family history disclosed that his father died at age 50 of "heart attack" shortly after the onset of severe "migraine headaches" and hypertension. A paternal aunt died at age 45 of "heart attack". Mother is alive with emphysema. Maternal grandparents died in "old age" of

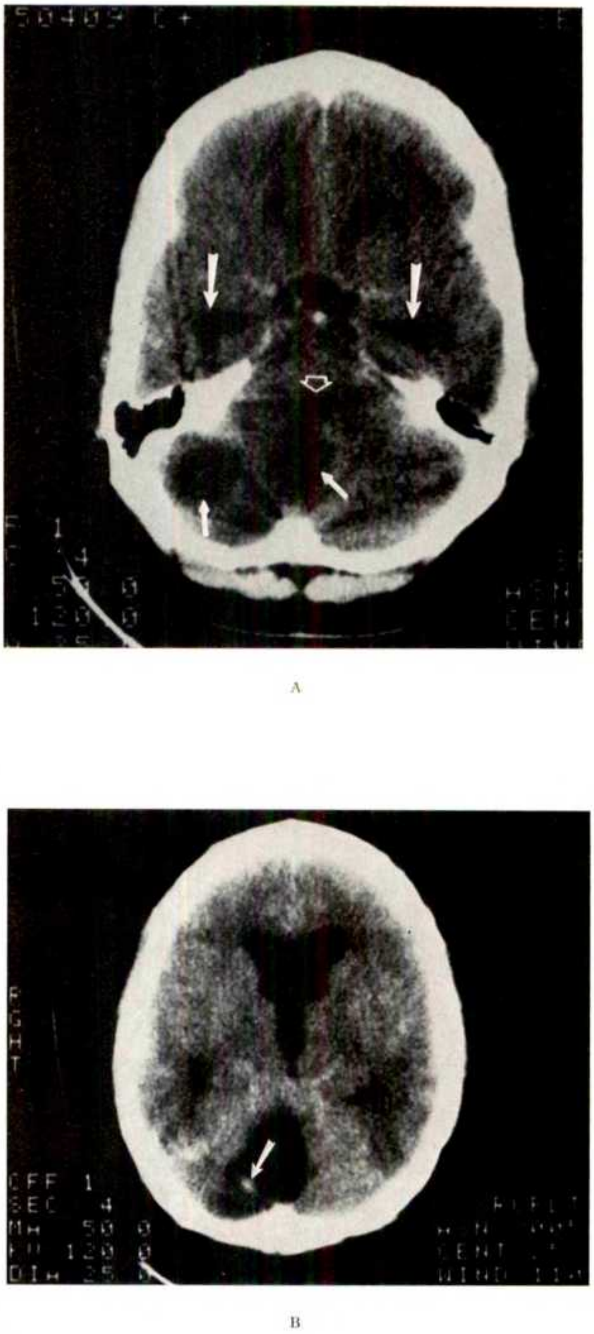


FIG. 1.

(A) Contrast-enhanced CT scan of the head on twin "A" demonstrates hypodense lesions consistent with cysts in the right cerebellar hemisphere (small arrows). The fourth ventricle (arrowhead) is distorted and displaced anteriorly. Moderate enlargement of the temporal horns is present (large arrows).

(B) Scan taken 2 cm above, showing a mural nodule in one of the cysts (arrow). Moderate ventricular enlargement is present.

"stroke". His identical twin is alive and well with amblyopia OS since childhood. Three female siblings are alive and well, one with a history of "collapsed lung". Physical examination was normal except for enlarged, tortuous vessels in both retinae. Fundus photography later showed bilateral retinal angiomas (Fig. 2). Bilateral vertebral arteriograms revealed six small hypervascular nodules in the cerebellar hemispheres and a "tight posterior fossa" (Fig. 3). A 2 cm hypervascular nodule in the upper cervical region opacified on the right vertebral injection only (Fig. 4). Renal arteriography disclosed avascular masses in the right kidney and a 3 cm mass in the left kidney with neovascularity. Computerized tomography of the abdomen revealed multiple cysts within the pancreas and right kidney and a solid mass in the left kidney. A suboccipital craniotomy and Torkildsen shunt were performed with excision of three large cysts containing mural haemangioblastomas from the right cerebellar hemisphere. A left radical nephrectomy was performed approximately one month later. Multiple pancreatic cysts were discovered and three separate small carcinomas were found in the left kidney along with multiple small cortical cysts. Laser photocoagulation treatments of both retinal angiomas were completed without visual loss. The patient is alive and

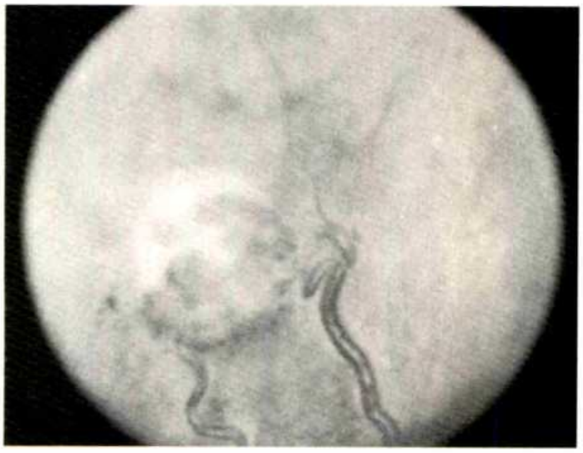


FIG. 2.

Fundus photograph on twin "A" showing a retinal angioma with enlarged artery and draining vein.

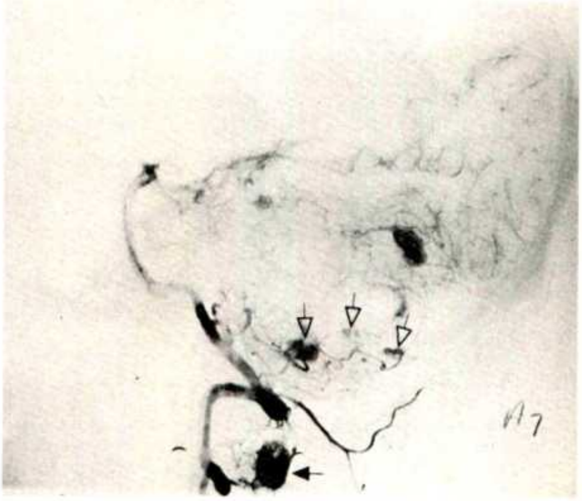


FIG. 4.

Right vertebral arteriogram on twin "A", mid-late arterial phase. Subtraction lateral view disclosing three additional hypervascular nodules in the cerebellum (hollow arrows) and a 2 cm nodule in the upper cervical region (solid arrow).

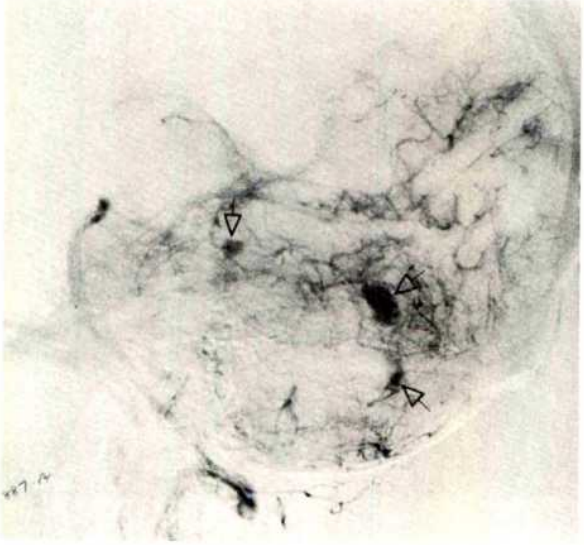


FIG. 3.

Left vertebral arteriogram on twin "A", late arterial phase. Subtraction lateral view disclosing three hypervascular nodules consistent with haemangioblastomas (arrows).

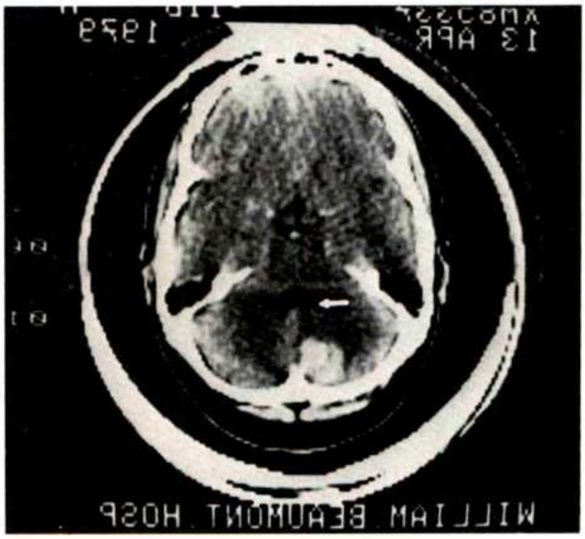


FIG. 5.

Contrast enhanced CT scan of the head on twin "B" disclosing a 2.5 cm enhancing lesion in the medial aspect of the left cerebellar hemisphere. There is mild distortion of the lateral recess of the fourth ventricle on the left (arrow).

well approximately 20 months after discharge. Interval abdominal CT examinations have shown no change.

Case 2: Twin "B"

This 27-year-old white male was completely asymptomatic at the time of his initial examination. He came to visit his twin while the consulting neurologist was present. Funduscopic examination revealed enlarged left retinal vessels and the patient was advised to see his personal physician. Fundus photography revealed a large left retinal angioma. Diminished vision, present since childhood, was diagnosed as amblyopia since no macular involvement by the angioma was present. IVU with tomography was reported as normal. Computerized tomography of the head revealed a 2.5 cm mass in the left cerebellar hemisphere and mild distortion of the fourth ventricle (Fig. 5). On physical examination, cysts of the left epididymis and very small pigmented naevi on the hands were discovered. A vertebral arteriogram revealed a 2.5 cm hypervascular mass in the left cerebellar hemisphere (Fig. 6). A renal arteriogram revealed two avascular masses in the left kidney consistent with cysts. Computerized tomography of the abdomen revealed three discrete lesions in the left kidney consistent with cysts (Fig. 7). Ultrasound guided aspiration of the two larger cysts yielded clear, straw-coloured fluid with negative cytology. Radiographs showed lobulation of one cyst wall. A suboccipital craniotomy and excision of a 2.5 cm haemangioblastoma from the left cerebellar hemisphere were performed. Follow-up CT of the abdomen six months later revealed enlargement and increased density of one of the left renal cysts. A pancreatic cyst was also seen (Fig. 8). A renal arteriogram revealed a 3 cm mass with neovascularity in the left kidney. Avascular masses were present in the upper and lower poles (Fig. 9A, B). At operation, aspiration of the pancreatic cyst yielded clear fluid with negative cytology. A left radical nephrectomy was performed. Sectioning of the gross specimen revealed a 3 cm "cyst within a cyst" in the upper pole, a 2.7 cm haemorrhagic nodule in the mid-portion and a 4 mm solid orange nodule beneath the capsule, and multiple small cortical cysts (Fig. 10). Microscopy demonstrated carcinoma in the two solid nodules and in the wall of the "cyst within a cyst". The cortical cysts had irregular contours of the lining with numerous papillary infoldings and areas of cuboidal clear cell lining, sometimes several layers thick, suggesting neoplastic proliferation. Follow-up CT of the abdomen at six-month intervals has disclosed no new masses.

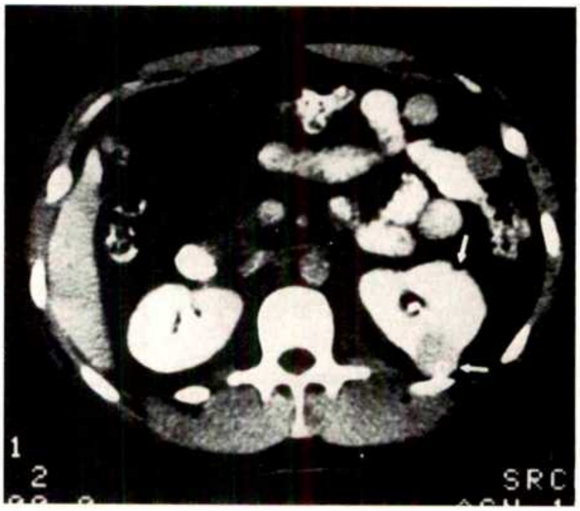


FIG. 7.

Initial contrast-enhanced CT scan of the abdomen on twin "B" disclosing discrete hypodense lesions arising from the cortex of the left kidney (arrows). A cursor is seen in the larger of the lesions. Density measurements were consistent with cysts.

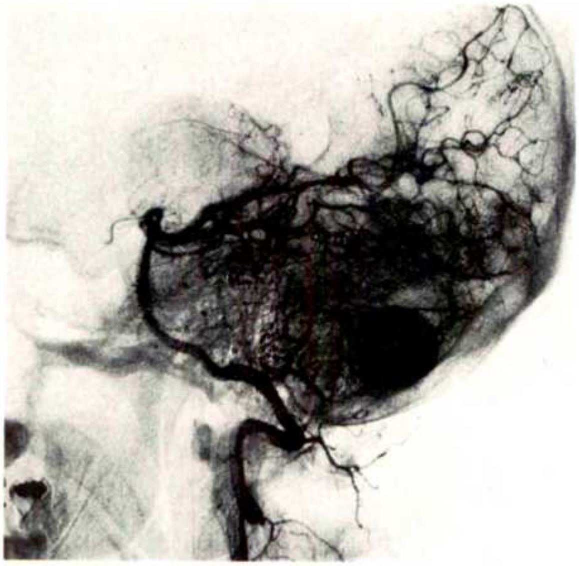


FIG. 6.

Left vertebral arteriogram on twin "B", late arterial phase. Subtraction lateral view disclosing a 2.5 cm hypervascular mass in the region of the left cerebellar hemisphere.

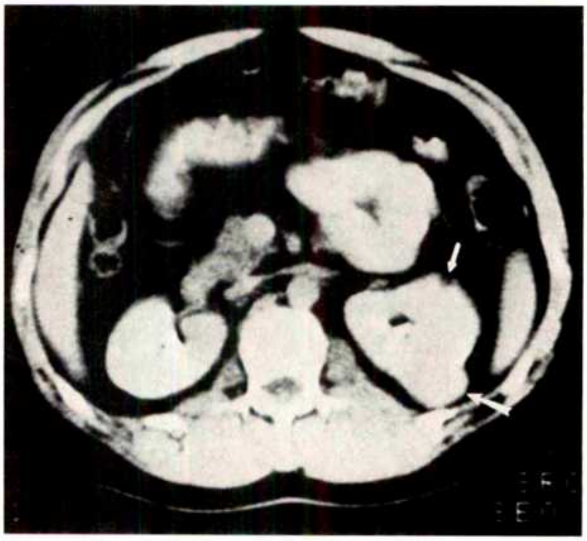
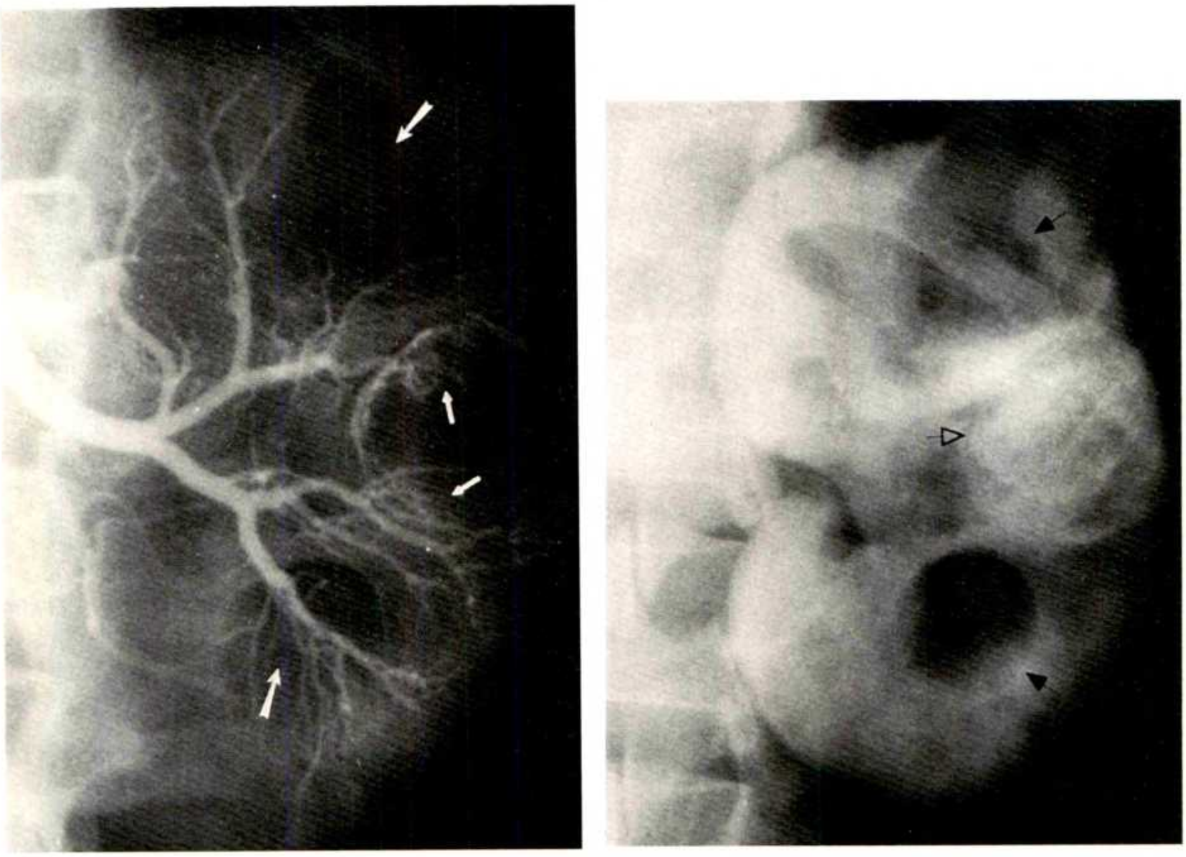


FIG. 8.

Six-month follow-up CT of the abdomen on twin "B" disclosing enlargement and increased density of the lesion in the postero-lateral aspect of the left kidney (large arrow). The small hypodense lesion on the anterior aspect of the kidney appears unchanged (small arrow).



A FIG. 9. B

(A) Selective left renal arteriogram performed on twin "B". Arterial phase discloses neovascularity in the mid-portion of the kidney (small arrows). Avascular masses are seen in the upper and lower poles (large arrows).

(B) Parenchymal phase discloses a solid tumour nodule in the mid-portion (open arrow) and well circumscribed avascular lesions consistent with cysts in the upper and lower poles (closed arrows).

Tissue cultures and chromosomal analyses of the haemangioblastomas removed from both patients were performed as part of an on-going study of chromosomal abnormalities in brain tumours. The karyotypes showed a Robertsonian translocation involving chromosomes 13 and 22 (45, XY, t' 13:22). Identical karyotypes were obtained from leucocyte cultures in both patients, as well as the mother and one sister, examined in the course of genetic counselling.

DISCUSSION

Contrast enhanced computed tomography of the head is a useful, non-invasive modality which should be used in the initial evaluation of patients suspected of having haemangioblastomas and in a symptomatic patient at risk for HLS. The larger solid tumours and cysts are well demonstrated along with associated mass effects including hydrocephalus. Occasionally, mural nodules are demonstrated. The angiographic findings in twin "A" support previous reports stating that arteriography is more sensitive and specific in defining the smaller nodules and characterizing the lesions (Seeger *et al.*, 1981) (Figs. 3, 4) Additionally, selective injection of both vertebral arteries is essential to evaluate fully for the presence of lesions in the cervical region which may receive their arterial supply from only one side (Fig. 4).

Multifocal renal cell carcinomas associated with multiple cortical cysts were discovered in both patients. Carconoma was present in twin "A" at the time of his initial presentation while twin "B" developed a solid mass from an apparent cyst approximately six months later and was shown to have carcinoma in the walls of other cysts. The reported incidence of renal carcinoma in patients affected with HLS ranges from 12 to 83% (Fill *et al.*, 1979; Lee *et al.*, 1977). The carcinomas are often multifocal, bilateral and contained within cysts (Pearson *et al.*, 1980). Careful evaluation of the kidneys is essential as soon as the patient is identified as being affected

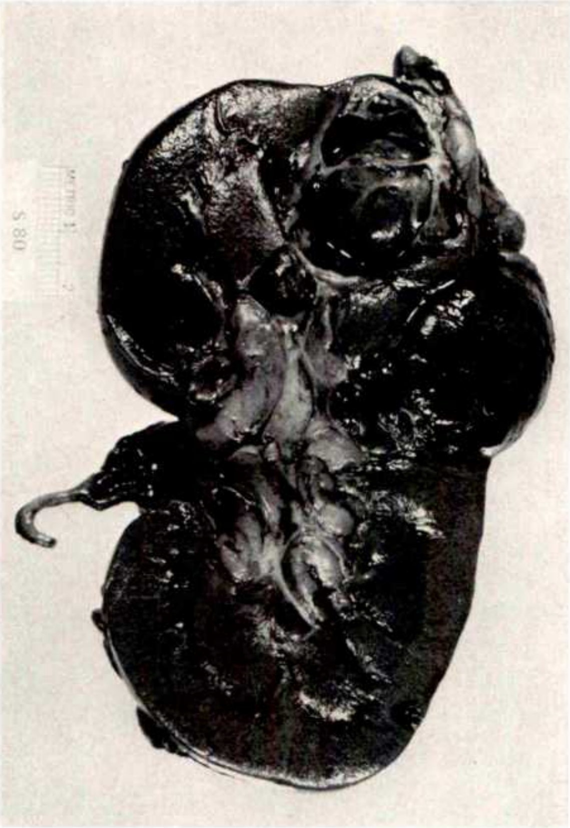


Fig. 10.

Photograph of the gross specimen removed from twin "B". A "cyst within a cyst" is seen in the upper pole, a haemorrhagic tumour nodule is seen in the mid-portion, and a small cortical cyst is seen in the lower pole.

with HLS. It is mandatory to perform renal arteriography in these patients even if intravenous urography and nephrotomography is negative. It is suggested that bilateral renal ateriograms be performed at the time of vertebral arteriography when feasible. The angiographer must be alert for hypertensive episodes which may occur in the presence of coexistent phaeochromocytomas (Hessel *et al.*, 1979).

Computerized tomography of the abdomen is a sensitive, non-invasive modality which can be used to screen asymptomatic patients for the development of carcinoma. It has been suggested that CT of the abdomen be performed as the initial screening test in patients at risk, followed by yearly scans if renal lesions are identified (Levine *et al.*, 1979). If other tests, such as ultrasonography or cyst aspiration, are equivocal, more frequent CT scans are necessary. A changing pattern of any lesion is an indication for renal arteriography.

Once an individual has been identified as affected by HLS, the other members of the family, especially twins, should be evaluated for the disease. The expression of HLS at earlier ages in subsequent generations has been observed in some of the studies of large affected families (Christoferson *et al.*, 1961; Lee *et al.*, 1977). Since the father and paternal aunt were presumably affected in their fifth decade and the two patients in this report were affected in their third decade, this phenomenon of genetic anticipation may have been present. It has been observed that patients harbouring brain tumours of different histological types have a higher incidence of numerical and/or structural chromosomal abnormalities involving chromosome 22 than can be explained on a statistical basis (AlSaadi and Latimer, 1980). What effect, if any, the presence of the abnormal karyotype in the present family had on the expression of the syndrome is conjectural. Further studies of posssible effects of chromosomal abnormalities on the expression of the syndrome may be helpful, particularly in regard to genetic counselling.

ACKNOWLEDGMENTS

The authors wish to thank the Departments of Neurosurgery, Ophthalmology, and Pathology, particularly the sections of Anatomic Pathology and Cytogenetics, for their assistance in preparing this report. We would also wish to thank the Audiovisual Department and Mrs. Kathryn Hurd for their assistance in preparing the manuscript.

REFERENCES

ALSAADI, A. and LATIMER, F. R., 1980. Non-random chromosomal abnormalities in human brain tumors. *American Journal of Human Genetics*, *32*, 61.

CHRISTOFERSON, L., GUSTAFSON, M. and PETERSON, A., 1961. Von Hippel-Lindau's disease. *Journal of the American Medical Association*, *178*, 280–282.

FILL, W. L., LAMIELL, J. M. and POLK, N. O., 1979. The radiographic manifestations of Von-Hippel Lindau disease. *Radiology*, *133*, 28,–295.

HESSEL, S. J., ADAMS, D. R. and ABRAMS, H. L., 1981. Complications of angiography. *Radiology*, *138*, 273–381.

HORTON, W. A., WONG, V. and ELDRIDGE, R., 1976. Von Hippel-Lindau disease. *Archives in Medicine*, *136*, 769–777.

LEE, K. R., WULFSBERG, E. and KEPES, J. J., 1977. Some important radiological aspects of the kidney in Hippel-Lindau Syndrome. The value of prospective study in an affected family. *Radiology*, *122*, 649–653.

LEVINE, E., LEE, K. R., WEIGEL, J. E. and FARBER, B., 1979. computed tomography in the diagnosis of renal carcinoma complicating Hippel-Lindau syndrome. *Radiology*, *130*, 703–706.

MELMON, K. L. and ROSEN, S. W., 1964. Lindau's disease. *Americal Journal of Medicine*, *36*, 595–617.

PEARSON, J. C., WEISS, J. and TANGAHO, E. A., 1980. A plea for conservation of kidney in renal adenocarcinoma associated with Von Hippel-Lindau disease. *Journal of Urology*, *124*, 910–912.

RICHARDS, R. D., MEBUST, W. K. and SCHIMKE, R. N., 1975. A prospective study on Von Hippel-Lindau disease. *Journal of Urology*, *110*, 27–29.

SEEGER, J. F., BURKE, D. P., KNAKE, J. E. and GABRIELSEN, T. O., 1981. Computed tomographic and angiographic evaluation of hemangioblastomas. *Radiology*, *138*, 65–73

1981, *British Journal of Radiology*, 54, 987–989 NOVEMBER 1981

An intracardiac foreign body: diagnosed non-invasively and removed non-surgically

By J. Davies, M.R.C.P., R. Alvares, M.D. and D. J. Allison, B.Sc., M.D., F.R.C.R.

Departments of Clinical Cardiology and Diagnostic Radiology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

(*Received February 1981*)

The hazards of retained catheter fragments are significant and in a recent review of the literature 16 well-documented fatalities were reported (Fisher and Ferreyro, 1978). In 12 of these 16 cases, catheter fragments were lodged in either the right atrium, the right ventricle, or both. Five patients died because of perforation of the heart; four from sepsis; three from pulmonary emboli; two from cardiac arrests secondary to arrhythmias, one from monilial endocarditis, and one from a perforated heart valve. The latter patient was also found to have a mycotic aneurysm of the pulmonary artery. Fisher and Ferreyro calculated the overall potential risk of death or serious complications from retained catheter fragments to be 71%. They emphasized that although patients may remain well initially, catastrophes can occur several months or even years after embolization.

CASE REPORT

A 27-year-old male Ghanaian was transferred from Accra to the Hammersmith Hospital with an 11-day history of abdominal pain followed by constipation, fever, dehydration and jaundice. On admission he was confused, pyrexial and jaundiced. His abdomen was distended and painful with ascites and massive hepatomegaly. Abdominal ultrasonography suggested the presence of five large cystic lesions in the liver, and hepatic angiography showed displacement of vessels around these lesions with no evidence of a tumour circulation. Percutaneous needle aspiration of one of these lesions yielded fluid containing large numbers of *Entamoeba histolytica*.

In view of the advanced nature of his illness, it was felt that surgical drainage of the abscesses coupled with metronidazole therapy was the treatment of choice. A laparotomy was performed and several large amoebic abscess cavities were evacuated. In the initial post-operative period the patient remained very confused and parenteral nutrition was administered through a central venous catheter (14G Bard catheter). This catheter was introduced through a large needle into an antecubital vein. The needle was withdrawn following the successful introduction of the catheter, a plastic needle guard positioned over the needle tip, and the catheter, guard and needle strapped firmly to the forearm. The patient remained seriously confused and one evening he pulled out his central line, snapping it and leaving behind 12 cm of catheter, which then migrated to the heart. A plain chest radiograph was reported as normal, but an echocardiogram strongly suggested the presence of a large foreign body within the right ventricle (Fig. 1). This finding was later confirmed by ciné-fluoroscopy which showed a 12 cm faintly radiopaque catheter fragment within the body of the right ventricle extending through the main pulmonary artery to the left pulmonary artery. As his general post-operative condition was still stabilizing and he had no immediate problems relating to this retained plastic catheter, it was decided that emergency removal of the retained fragment was not necessary.

The patient had made excellent progress on metronidazole following surgical drainage and two months later a repeat ultrasound study showed that his liver had returned virtually to normal. Five weeks post-operatively, when he was well and asymptomatic, he was readmitted for an elective transvenous removal of the retained intracardiac catheter.

When a radiological technique is used for the removal of retained intravascular fragments they are usually retrieved by slipping a wire snare over one end of the fragment. This method could not be employed in the present case, however, as both ends of the retained piece were apparently embedded in endothelial surfaces and a modified technique was devised for its removal. An endocardial biopsy sheath (9 French gauge) was introduced through a right femoral venotomy. A catheter with a deflectable tip (Medi-tech), was passed through the sheath until it protruded 5 cm beyond its tip. Catheter and sheath were then advanced together to the right ventricle; the free deflectable tip was wound tightly round the retained catheter fragment and then pulled back against the sheath so that the captured fragment could not escape. Sheath, steerable catheter and retained fragment were then withdrawn together through the femoral venotomy (Fig. 2). So far as we are aware this technique has not been described previously. Recovery from the procedure was uneventful.

DISCUSSION

Extreme care must be employed when indwelling catheters are used in confused patients. Even when the needle used for introducing the catheter is correctly sheathed (as it was in the present case), the patient can cause the needle guard to become detached, and this may result in the catheter becoming severed. Attention has been drawn to this hazard in a recent Medical Defence Union Report (1979), and there have been previous reports of similar complications (John, 1972). Consideration should clearly be given to the correct choice of catheter and introducing system in seriously confused or unco-operative patients.

The first recorded case of embolization of a catheter fragment was in 1954 (Turner and Sommers). Surgical removal was the only method available until 1964, when a steel guide wire fragment was removed non-surgically from the right atrium (Thomas *et al.*), following which the transvenous technique was quickly adopted by others (Dotter *et al.*, 1971). The technique described in the present

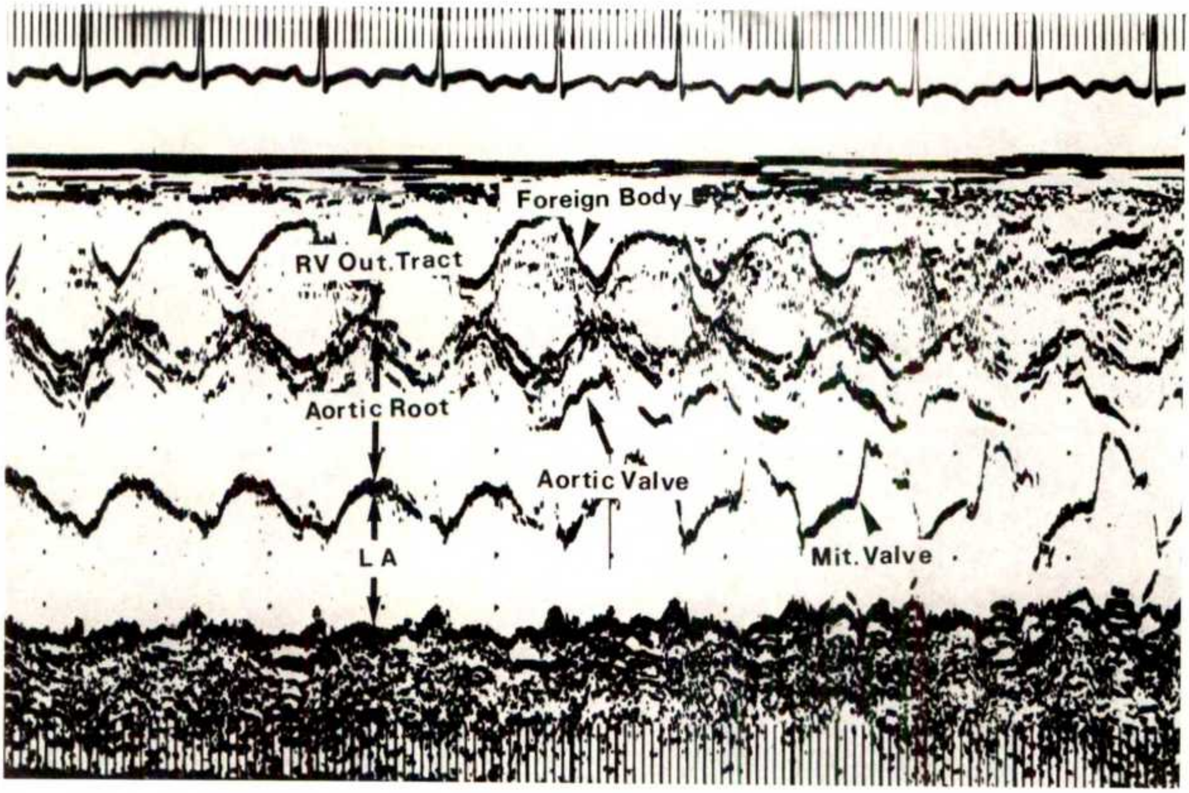


Fig. 1.

An echocardiographic "sweep" from aortic root to left ventricle showing continuous bizarre extraneous echoes within the body of the right ventricle extending to the right ventricle outflow tract. The echocardiogram is otherwise normal.

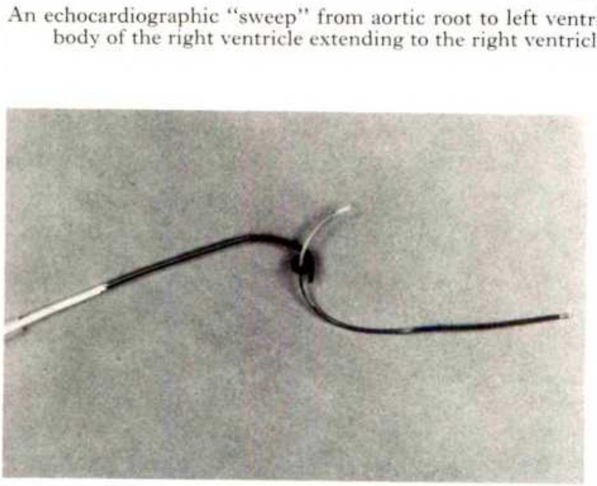


Fig. 2.

Post-removal photograph showing the fragment of detached catheter ensnared by the tip of the steerable catheter.

case for removal of the retained fragment does not require either end of the fragment to be accessible to the operator, since the deflectable tip catheter can be wound round any part of the retained fragment. It is a particularly suitable method, therefore, in cases where the ends of the retained fragment are embedded in endothelium, or anatomical structures such as valves, and in cases where the retained fragment is only faintly radiopaque, making fluoroscopic identification of a free end of the fragment extremely difficult.

Temporary and permanent pacemaker wires have frequently been demonstrated on the echocardiogram but the detection of a "lost" intravenous plastic feeding catheter by this method has not previously been reported. These catheters are only faintly opaque and a detached fragment may be undetectable on a standard chest radiograph if, as in the present case, it lies within the dense cardiac silhouette. We would therefore suggest that echocardiography may be a simple, quick and non-invasive aid to diagnosis if this problem is suspected.

Acknowledgment

We thank Professor D. K. Peters for allowing us to report a patient under his care.

REFERENCES

Fisher, R. G. and Ferreyro, R., 1978. Evaluation of current techniques for nonsurgical removal of intravascular

iatrogenic foreign bodies. *American Journal of Roentgenology*, *130*, 541–548.
JOHN, G. E., 1972. DHSS Hazard Notice 6, (DS) (S) 6/72.
MEDICAL DEFENCE UNION, 1979. Another intravenous catheter. Annual report, 1979, p. 21.
TURNER, D. D. and SOMMERS, S. C., 1954. Accidental passage of a polyethylene catheter from cubital vein to right atrium: report of a fatal case. *New England Journal of Medicine*, *251*, 744–745.
THOMAS, J., SINCLAIR-SMITH, B., BLOOMFIELD, D. and DAVACHI, A., 1964. Nonsurgical retrieval of a broken segment of steel spring guide from the right atrium and inferior vena cava. *Circulation*, *30*, 106–108.
DOTTER, C. T., ROSCH, J. and BILBAO, M. K., 1971. Transluminal extraction of catheter and guide fragments from the heart and great vessels: 29 collected cases. *American Journal of Roentgenology*, *111*, 467–472.

Cementifying fibroma (so-called "cementoma") of tibia

By *J. J. Kolář, M.D., Sc.D., †V. Horn, M.D., Sc.D., *H. Zídková, M.D. and *J. Šprindrich, M.D., Sc.B.

*Clinic for Diagnostic Radiology ILF, 180 81 Praha 8, Budínova 2 and †Bone Tumour Registry, University Hospital Brno, Pekařská 53, Czechoslovakia

(*Received April 1981*)

Cementifying fibroma of long tubular bones is an extremely rare condition known also by the name of a "cementoma" otherwise used for tumours of true dental origin in the jaws (Adkins *et al.*, 1976). It has been reported in less than ten children or adolescents, mostly in the femur or humerus. The lesion usually occupies the whole diameter of the bone, mostly the meta-diaphysis and has a radiographic appearance of a multi-cameral bone cyst. Some dense areas may be seen within this translucency, sometimes close to its inner surface.

CASE REPORT

A 24-year-old man presented in April 1979 with pain of three years' duration, which did not disappear after the removal of a loose body, due to osteochondritis dissecans, and a torn internal meniscus from the left knee in 1978. At physical examination, a slight prominence, not apparent, was felt on the anterior tibial surface. Clinical and laboratory reports were otherwise normal. Radiographically (Fig. 1) a central, 10 cm long cystoid radiolucent lesion with expansion was found in the upper tibial diaphysis, delineated by a sclerotic margin. It was incompletely divided by septa and contained several dense deposits. Angiographically (Fig. 2) somewhat broader arterial vessels were straightened over the tumour area, due to its expansion. No pathological vessels, precocious venous return or a positive tumour stain were noted.

The lesion was curetted on May 22, 1979. The cavity contained a mixture of loose tissue with harder remnants and a small amount of fluid. The defect was packed with bone chips and the patient made an uneventful recovery with no subsequent trouble at the last review in 1981.

Microscopically (Figs. 3 and 4) a differently proliferating fibrous tissue was found with dense cementicles which did not exhibit any close relation to fibroblasts. Their concentric structure and separation from adjacent cells support the conclusion that the cementicles arise in the intercellular matrix due to non-explained physico-chemical influences.

DISCUSSION

"Cementomas" of long bones have been described both clinically and microscopically by Friedman and Goldman (1969), Spjut *et al.* (1974) and Mirra *et al.* (1978). All their patients were under the age of 20 years and the lesion was localized in the upper metaphysis of femur or humerus, causing a pathological fracture. Microscopically, the lesions contained a peculiar, poorly cellular substance which mimics tooth cementum by light microscopy only. Friedman and Goldman (1969) believed that due to the embryonic multipotentiality of neoplastic cells and mainly metaphyseal cells in young individuals a cementum-producing response to environmental influences may be induced. Also Mirra *et al.* (1978) consider this entity not a separate entity; they believe it is a peculiar form of a bone cyst. Electron-microscopic studies of the cementum-like substance demonstrate collagen fibres and numerous matrix vesicles at the initial sites of calcification of such "cementicles". Such vesicles are never found in true cementum in the jaws.

This new observation of this rare entity differs from others by its localization (diaphysis of a long bone, not a metaphysis) and a somewhat higher age of the patient (usually the tumours were encountered after a fracture before the age of 20). Radiographic appearances and microscopic findings are otherwise consistent with the findings reported by the above-mentioned authors. For the first time an angiographic picture of this lesion is documented in the literature, showing its benign nature. Until now, a

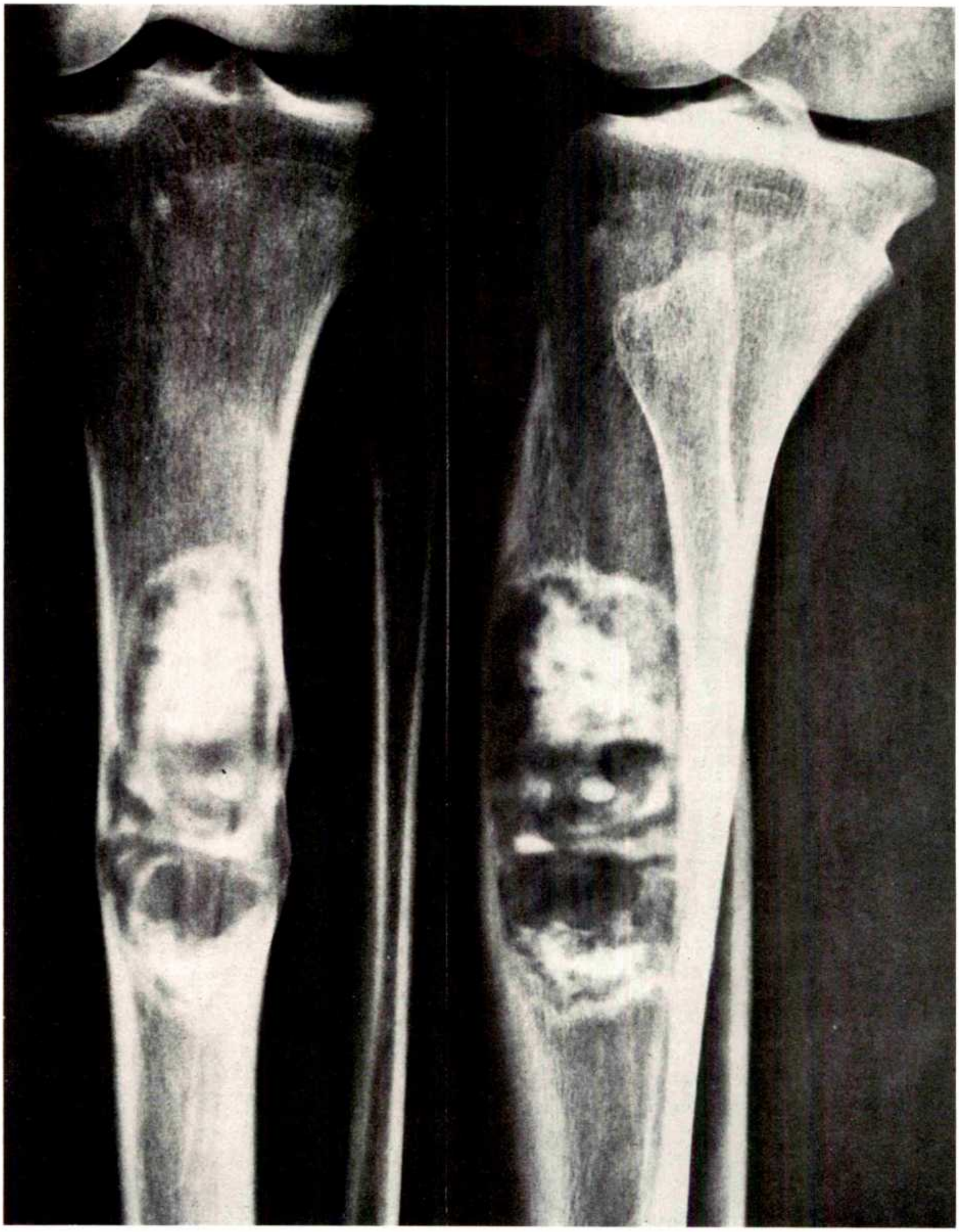


Fig. 1.

AP and lateral plain films show an expanding transluscent central lesion with a sclerotic border in the proximal tibial diaphysis. Incomplete septa and several densities within the tumour area.

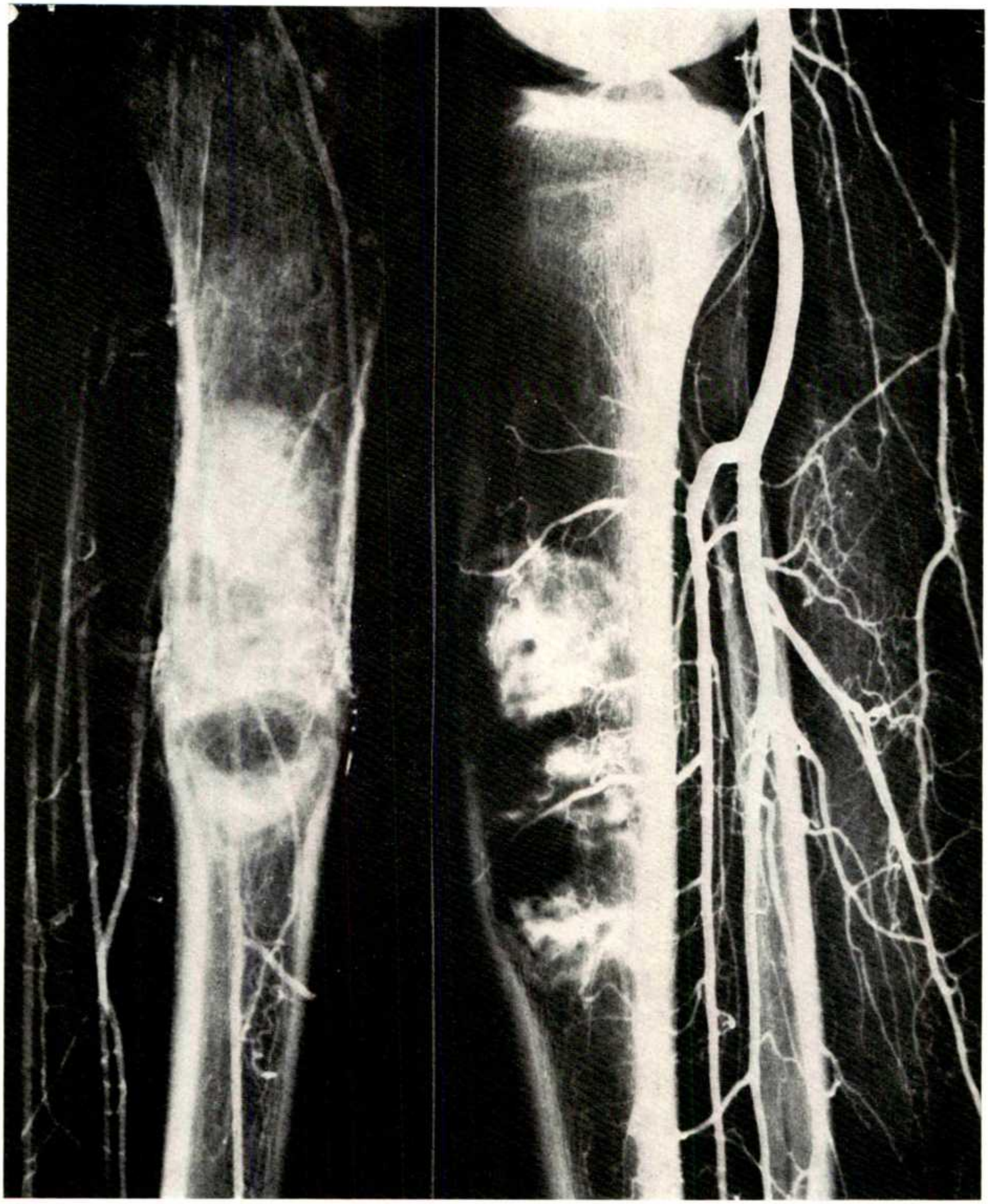


FIG. 2.

The capillary phase of an AP angiogram documents periosteal hypervascularization at the level of the expansion. The early arterial phase on the lateral angiogram shows an increased number of dilated arteries, running to the tumour area and straightened over it.

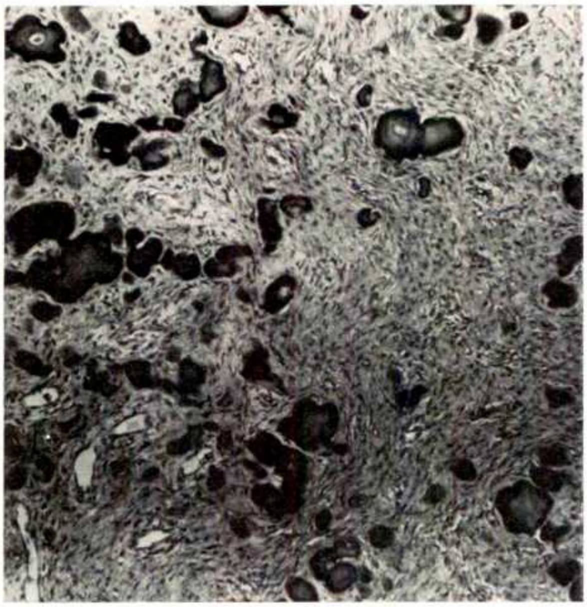


Fig. 3.

The cellular part of the cementifying fibroma with proliferating fibroblasts and basophilic oval and dentate cementum-like formations (HE stain, × 320).

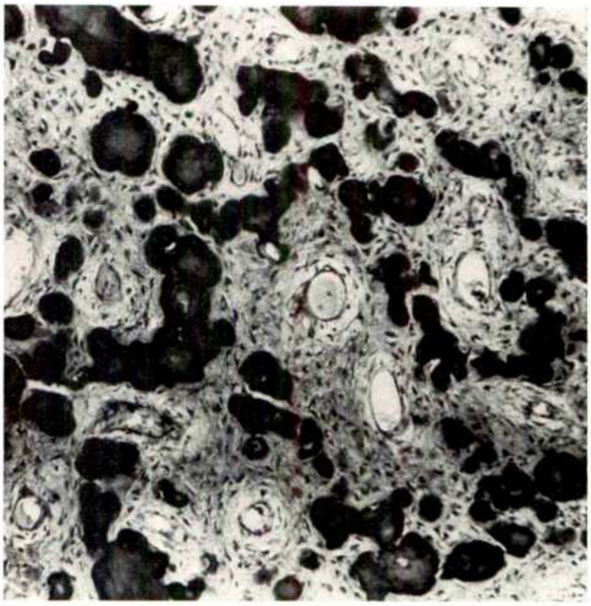


Fig. 4.

The less cellular fibrous part of the lesion with highly mineralized "cementicles" (HE stain, × 320).

pathological fracture was the only complication ever reported in the world medical literature of this benign lesion. The microscopic examination of our patient allows the postulate that it has nothing to do with a true "cementoma" in the jaws and it should be considered as an independent entity with a possible linkage to bone fibromas.

Acknowledgment

We would like to thank Dr. Zd. Matějovský, C.Sc., who operated on this patient.

REFERENCES

Adkins, W. J., Jr., Putney, F. J. and Kreutner, A., 1976. Cemento-osteoid tumour of the maxillary sinus. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, *82*, 563–567.

Friedman, N. B. and Goldman, R. L., 1969. Cementoma of long bones. *Clinical Orthopaedics*, *67*, 243–248.

Mirra, J. M., Bernard, G. W., Bullough, P. G., Johnston, W. and Mink, G., 1978. Cementum-like production in solitary bone cysts (so-called "cementoma" of long bones). *Clinical Orthopaedics*, *135*, 295–307.

Spjut, H. J., Dorfman, H. D., Fechner, R. E. and Ackerman, L. V., 1974. Tumors of bone and cartilage. *Atlas of Tumor Pathology*. 2nd Series, Fascicle 5 (Washington, Armed Forces Institute of Pathology).

Metastatic disease to the carpus

By P. C. Cary, M.D.

Department of Radiology, Pease Hospital, Pease AFB, NH 03801

C. A. Helms, M.D. and H. K. Genant, M.D.

Department of Radiology, University of California, San Francisco, San Francisco, CA 94143, USA

(Received May 1981)

Metastatic disease, previously believed not to occur distal to the elbow and knee, has been well documented in the phalanges (Kerin, 1958; Gold and Reefe, 1963; Mangini, 1967; Wu and Guise, 1978; Vancura *et al.*, 1960). Bronchogenic carcinoma is frequently the associated primary tumour (Kerin, 1958). However, at least one well known current textbook still states that metastases to the carpus are unknown (Greenfield, 1975). This paper presents a review of the world literature as well as three new cases of carpal metastases.

CASE REPORTS

Case 1

A 32-year-old woman with infiltrating ductal carcinoma of the right breast had four of 28 positive lymph nodes and a negative bone scan at the time of surgery. Fourteen months later she presented with pain in the right thumb, a positive bone scan in that area, and the radiographs shown in Figs. 1 and 2. Biopsy and subsequent surgical removal of the trapezium confirmed the presence of metastatic breast carcinoma.

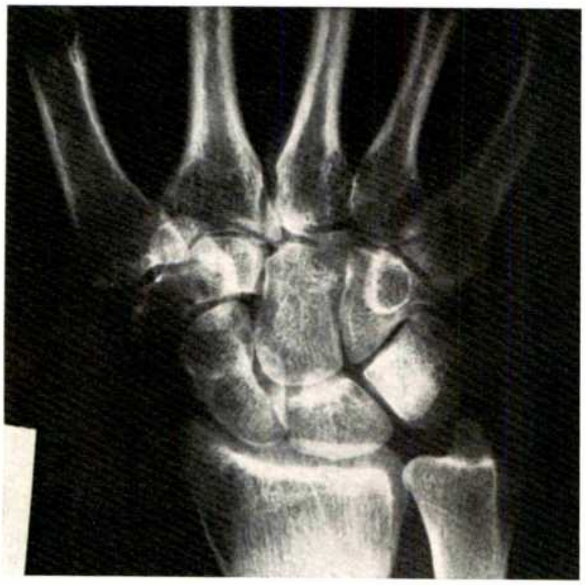


FIG. 1. *Case 1.*

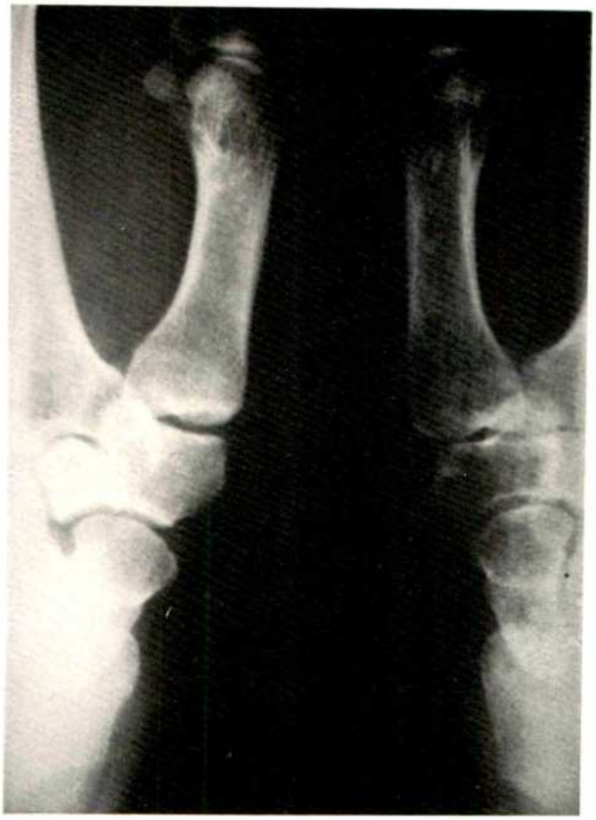


FIG. 2. *Case 1.*

Note the osteolytic destructive involvement of the proximal radial aspect of the trapezium with absence of the bony cortex. There is also prominent distal osteoporosis.

Case 2

A 54-year-old man with known bronchogenic carcinoma of the lung complained of left wrist pain. Radiographic examination was normal. Repeat examination four months later (Fig. 3) showed destruction of the lesser multangular and distal capitate, with disuse osteoporosis of the phalanges. Biopsy revealed metastatic carcinoma of the lung.

Case 3

A nine-year-old female with osteogenic sarcoma of the distal right femur presented with left wrist pain. A film of the carpus (Fig. 4) showed an osteoblastic lesion of the scaphoid with diffuse osteoid proliferation on the radial side. Surgery confirmed the diagnosis of osteogenic sarcoma.

DISCUSSION

The discovery of metastatic disease to the hand is no longer a rarity; indeed, lesions of the distal phalanx now elicit a suspicion which has led to the discovery of many occult pulmonary malignancies (Kerin, 1958). However, destructive or osteoblastic processes in the carpus do not routinely raise the same possibilities, probably because of their relative infrequency. Of 3000 patients with malignancies, only two had metastases to the hand (Gold and Reefe, 1963), and in the world literature, we are aware of a total of only six previously reported cases

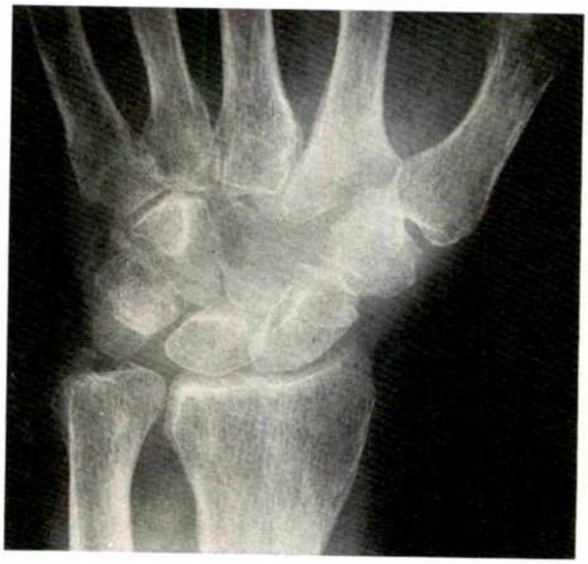


FIG. 3. *Case 2.*

There is marked destruction of the distal capitate and trapezoid, with surrounding osteoporosis.

TABLE I

Case	Author	Appearance	Site	Primary tumour
1	Vancura *et al.*	Osteolytic	Proximal left scaphoid	Lung
2	Kerin	Osteolytic	Right scaphoid capitate, trapezium and trapezoid	Breast
3	Smith	Osteolytic	Right trapezoid	Lung
4	Lochovsky and Pavlanski	Osteolytic	Left lunate	Lung
5	Wu and Guise	Osteoblastic	Right scaphoid	Humerus
6	Dolich *et al.*	Osteolytic	Scaphoid, trapezium and triquetrum	Lung
7	Cary *et al.*	Osteolytic	Right trapezium	Breast
8	Cary *et al.*	Osteolytic	Left trapezoid and capitate	Lung
9	Cary *et al.*	Osteoblastic	Left scaphoid	Femur

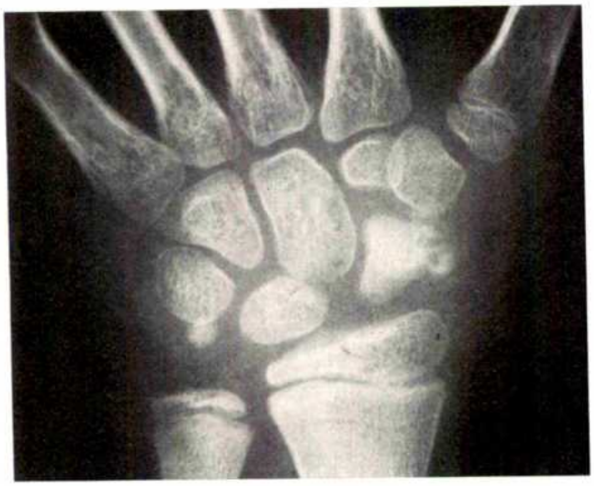


FIG. 4. *Case 3.*

Osteoblastic increased density characterizes this scaphoid, with prominent proliferative new bone extending radially and distally into the carpal joint space.

involving the carpus (Kerin, 1958; Mangini, 1967; Vancura *et al.*, 1960; Dolich *et al.*, 1970; Lochovsky and Pavlanski, 1966). To this we add three new cases; the sites of involvement, radiographic appearance, and primary tumour are indicated in Table I.

Several facts emerge from this. Seven of the nine (78%) are purely osteolytic, destructive lesions. The osteoblastic lesions both represented osteogenic sarcoma. While it is theoretically conceivable that these two represent second primary malignancies, the unusual location and presence of these metastatic lesions elsewhere both support their being carpal metastases.

Of the seven osteolytic carpal lesions, five were from a lung primary and the remaining two metastasized from the breast. Thus the lung represented the source of the carpal metastasis in five of nine cases (56%), a finding commensurate with the overall frequency reported in the hand (48%).

The differential diagnosis of a carpal lesion is facilitated by assessing osteolytic and osteoblastic appearances separately. Osteolytic destructive lesions of the carpus most commonly represent ostoemyelitis. Pyogenic infection can be expected in most cases to show a more rapid course, while an indolent infection may be characterized by more widespread osteoporosis and perhaps sclerotic margination. Clinical evidence will obviously be helpful in differentiation.

Geodes, or subchondral cysts, show a well-delineated sclerotic border, and are associated with rheumatoid arthritis, degenerative disease, aseptic necrosis, and calcium pyrophosphate deposition disease. The sharp margination and ancillary findings of these entities allow differentiation from metastasis.

Sclerotic lesions of the carpus with new bone formation are suggestive of osteogenic sarcoma, either primary or metastatic. Osteoid osteoma may produce dense cortical bone, with or without a central translucent nidus, but will not show an osteoid matrix in the adjacent joint spaces. Chronic osteomyelitis, in the form of a Brodie's abcess, closely mimics osteoid osteoma, but again without adjacent osteoid matrix. Avascular necrosis presents as a dense carpal bone or fragment of a carpal bone, but osteoid is again absent and an appropriate history such as antecedent trauma or corticosteroid therapy is usually present. Finally, Paget's disease characteristically causes bony enlargement, and may be osteolytic, osteosclerotic, or mixed. Paget's disease does not produce an osteoid matrix unless it has undergone sarcomatous degeneration.

REFERENCES

DOLICH, B. H., SPINNER, M. and KAUFMAN, G., 1970. Isolated metastasis to the carpal bones: report of a case. *Bulletin of Hospital Joint Disease*, *31*, 78–84.

GOLD, G. L. and REEFE, W. E., 1963. Carcinoma and metastases to the bones of the hand. *Journal of the American Medical Association*, *184*, 237–239.

GREENFIELD, G., 1975. *Radiology of bone diseases*, 2nd Edit. (Lippincott, Philadelphia), p. 328.

KERIN, R., 1958. Metastatic tumours of the hand. *Journal of Bone and Joint Surgery*, *40*, 263–278.

LOCHOVSKY, J. and PAVLANSKY, R., 1966. Metastasis in the os lunatum as the 1st symptom of bronchogenic carcinoma. *Acta Chirurgiae Orthopaedicae Traumatologiae Čechoslovaca*, *35*, 387–390.

MANGINI, U., 1967. Tumours of the skeleton of the hand. *Bulletin of Hospital Joint Disease*, *28*, 61–103.

SMITH, R., 1967. Involvement of the carpal bones with metastatic tumour. *American Journal of Roentgenology*, *89*, 1253–1255.

VANCURA, J., JAKOUBKOVA, J. and KOLAZ, J., 1960. Die Metastasen in kleinen Handknochen beim Lungenkrebs. *Zentralblatt für Chirurgie*, *85*, 1554–1557.

WU, K. and GUISE, E., 1978. Metastatic tumours of the hand: a report of six cases. *Journal of Surgery*. *3*, 271–276.

Hypothenar hammer syndrome

By D. R. Foster, D.M.R.D., F.R.C.R. and D. C. Cameron, M.R.C.P., F.R.C.R., M.R.A.C.R.

Department of Diagnostic Radiology, Royal Perth Hospital, Wellington Street, Perth, Western Australia

(*Received April 1981*)

Recurrent blunt trauma to the palm of the hand may result in trauma to the ulnar artery. The combination of signs and symptoms of ischaemia of the hands and fingers secondary to recurrent trauma has been termed the hypothenar hammer syndrome. Constant striking of the hypothenar eminence hammers the distal ulnar artery and its superficial palmar branch against the hook of the hamate bone. Pathologically this will result in arterial spasm, thrombosis or aneurysm formation. The syndrome was first described by Conn *et al.* (1970), who noted the relationship with occupational trauma in their series of 11 patients. We have recently encountered two further cases which illustrate the typical appearances and value of arteriography in this condition.

CASE REPORTS

Case 1

A 31-year-old carpenter presented with a one-week history of progressive coldness and tingling in the right ring and little fingers. He used his hand as a "hammer" frequently during work. On examination the right ring and little fingers were cool and there was cyanosis along the ulnar border of the little finger. Radial and ulnar arterial pulses at the wrist were normal. Arteriography via the transfemoral route demonstrated a normal aortic arch and axillary artery. Angiograms of the hand using warming of the distal limb, a vasodilator and macroradiographic technique confirmed occlusion of the distal ulnar artery just proximal to the hook of the hamate (Fig. 1). There was also non-filling of the 5th digital artery. The patient was subsequently treated by sympathectomy with good result.

Case 2

A 40-year-old man was admitted with a one-week history of paraesthesiae in the right middle finger. Five days prior to admission he had noticed discoloration of the skin of this finger. He worked as an engineer and had experienced repeated minor trauma to his hand in the past. Examination revealed bluish discoloration of the skin over the distal right middle and little fingers. All pulses were normal. Arteriography (Fig. 2) showed poor filling of the distal arteries of the middle finger with occlusion of the ulnar artery adjacent to the hook of the hamate. The patient made progressive improvement following sympathectomy.

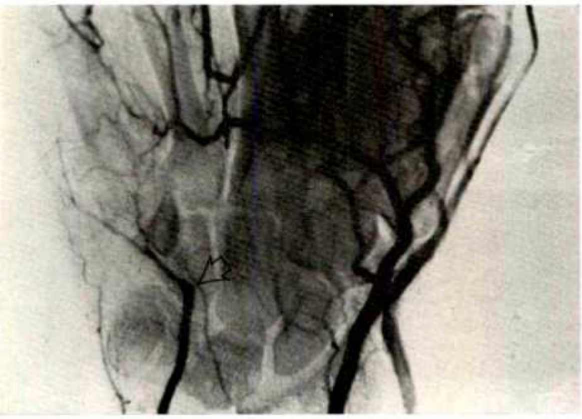


FIG. 1.

Occlusion of ulnar artery proximal to the hook of the hamate (arrow). Non-filling of superficial palmar arch.

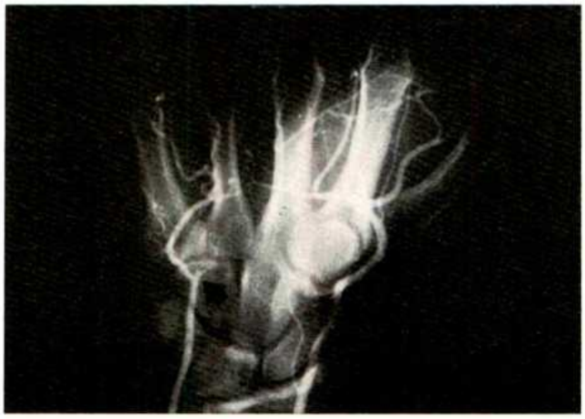


FIG. 2.

Occlusion of ulnar artery proximal to the hook of the hamate (arrow). Non-filling of superficial palmar arch. Marked narrowing of deep palmar arch adjacent to 4th metacarpal.

ANATOMY

The normal angiographic anatomy of the hand was reviewed by Calenoff (1972). The anatomy is complex and subject to individual variation. The common palmar digital arteries provide the major blood supply to the fingers. They arise in the metacarpal spaces from the superficial palmar arch. The latter is the major terminal branch of the ulnar artery which bifurcates into superficial and deep palmar branches in a groove (Guyon's tunnel) bounded medially by the pisiform bone and hook of the hamate and laterally by the transverse carpal ligament. For its proximal 2 cm it is vulnerable to trauma, being superficial in the palm covered only by skin, subcutaneous tissues and the palmaris brevis muscle. The superficial arch is present and complete in 70% of individuals, joining the superficial palmar branch of the radial artery. The deep palmar arch is a major terminal branch of the radial artery. It gives rise to a number of palmar metacarpal arteries which anastamose with common palmar digital arteries. The deep palmar arch is less variable than the superficial, being complete in over 90% of cases.

The occurrence of ischaemic symptoms following occlusion of the ulnar artery or its superficial palmar branch will depend on the completeness of the arch as well as upon collateral circulation from terminal branches of the radial artery.

DISCUSSION

Symptomatic digital ischaemia involving the dominant hand of a male patient who presents with a history of recurrent minor blunt trauma to the hand suggests the diagnosis of the hypothenar hand syndrome. Little and Ferguson (1972) noted that ulnar artery occlusion is not uncommon in populations subjected to occupational trauma, although symptoms may not be severe enough to seek medical advice. They studied 79 mechanics who admitted to recurrent "hammering" using their palms. In 11 of these men, Doppler flow detection studies showed evidence of ulnar artery occlusion. All admitted to mild symptoms often exacerbated by cold but none showed objective evidence of ischaemia.

Arteriography is necessary for anatomical localization and confirmation of the diagnosis although Doppler detection only was preferred by one group (Kleinert and Volianitis, 1965). Brachial arteriography was used by Benedict *et al.* (1974) but we prefer a transfemoral approach since a cause of proximal arterial disease can be excluded by arch aortography and selective axillary arteriography when necessary. We have also found vasodilator drugs and warming of the affected hand useful in obtaining fine detail. The typical angiographic abnormality is occlusion of the ulnar artery at the point where the vessel crosses the hamate bone. Other features can include occlusion of the superficial palmar arch and single or multiple digital artery occlusions.

Although the use of stellate ganglion block has provided temporary improvement, the surgical treatment of choice is sympathectomy. Good postoperative results were obtained in both our cases using this technique.

ACKNOWLEDGMENTS

We would like to thank Dr. Glenn Scott who performed the arteriogram in Case 2, and also the vascular surgeons of Royal Perth Hospital for permission to report these cases.

REFERENCES

BENEDICT, K. T., CHANG, W. and MCREADY, F. J., 1974. The hypothenar hammer syndrome. *Radiology*, *111*, 57–60.

CALENOFF, L., 1972. Angiography of the hand; Guidelines for interpretation. *Radiology*, *102*, 331–335.

CONN, J., BERGAN, J. J. and BELL, J. L., 1970. Hypothenar hammer syndrome: post-traumatic digital ischaemia. *Surgery*, *68*, 1122–1128.

KLEINERT, H. E. and VOLIANITIS, G. J., 1965. Thrombosis of the palmar arterial arch and its tributaries: aetiology and newer concepts in treatment. *Journal of Trauma*, *3*, 447–457.

LITTLE, J. M. and FERGUSON, D. A., 1972. The incidence of the hypothenar hammer syndrome. *Archives of Surgery*, *105*, 684–685.

The importance of radiological monitoring after oesophageal intubation

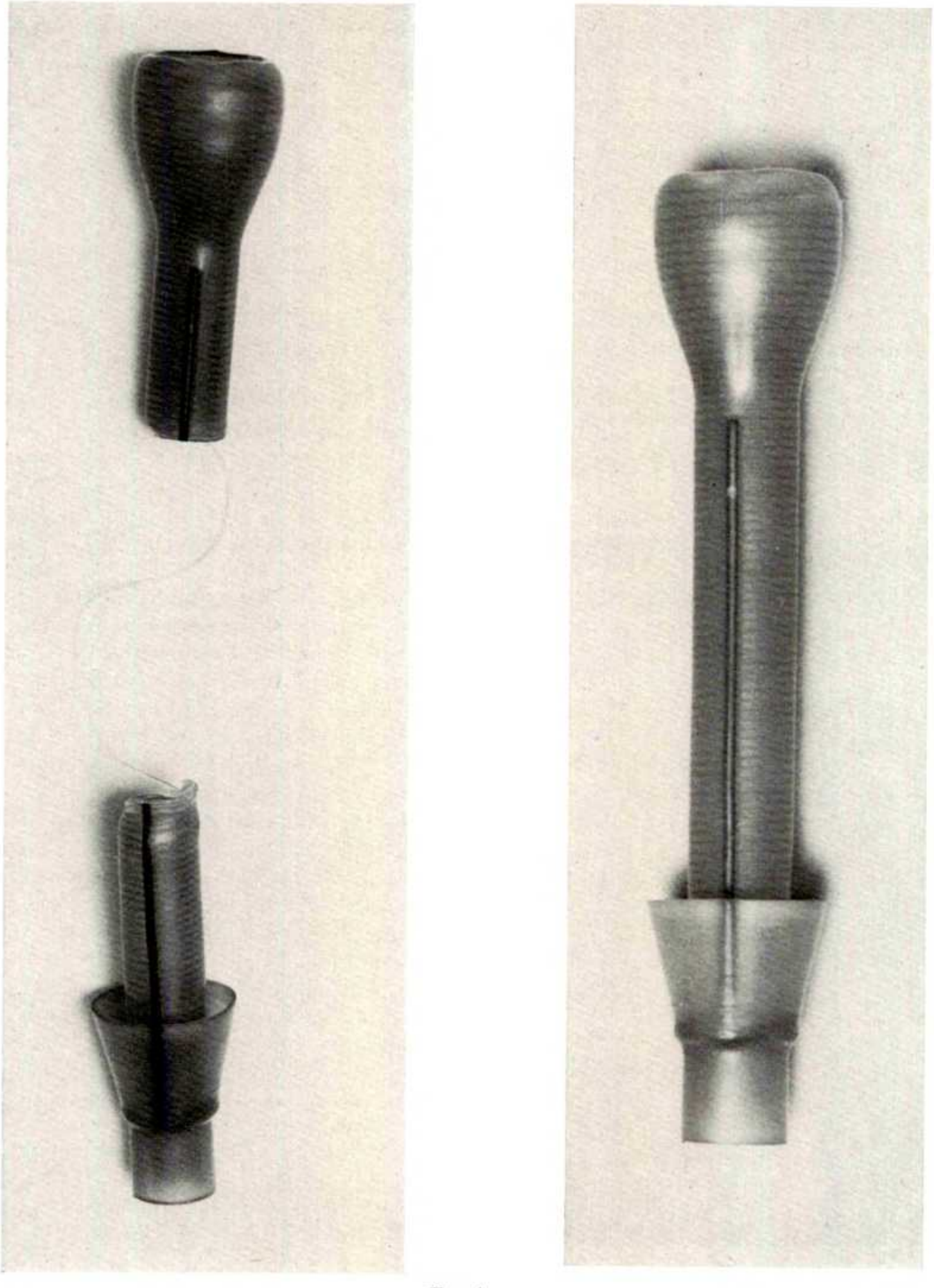
By *W. B. Campbell, M.R.C.P., F.R.C.S. and †D. J. Mackenzie-Crooks, M.R.C.P., F.R.C.R.

Departments of *Surgery and †Radiology, Frenchay Hospital, Bristol, BS16 1LE

(Received May 1981)

Celestin pulsion and traction tubes (Celestin, 1959; 1978) are frequently used in the treatment of both malignant and benign strictures of the oesophagus. Occasional late complications of intubation include dislodgement of the tube, which may be passed intact from the anus, and also fragmentation of the tube (Mackenzie *et al.*, 1976; Rao, 1978; Brown and Hughes, 1979; MacGowan, 1980) which may have serious consequences.

Radiological monitoring of the position and integrity of these tubes is made possible by the presence of a single radiopaque marker line in some models, while others are radiopaque throughout. The tubes are made of activated latex rubber, reinforced by a tightly wound spiral of nylon (Fig. 1A); following tube fracture the nylon unwinds but



A FIG. 1. B

Celestin pulsion tube. (A) Intact tube. (B) Fractured tube showing intact connecting nylon thread.

remains intact to form a connection between the two fragments (Fig. 1B). As the distal fragment passes down the bowel, the nylon may become taut within the lumen and lead to pressure necrosis of the wall—the so-called "cheese-wire" effect. This may then go on to perforation (Shaw and Coombes, 1979; Laughlin and Walker, 1980; Meyer and Zannit, 1980). Radiological diagnosis of tube fracture is therefore of the greatest importance, in order that early operation may be performed in these cases. Such diagnosis is a simple matter if a large portion of the tube has passed distally, but if a small fragment has separated, only a high index of suspicion and careful radiological search may reveal the complication.

We describe a case of migration and fracture of a Celestin tube following which the patient died. Post-mortem examination revealed full thickness necrosis of the small bowel wall with peritonitis.

Case Report

A 79-year-old man presented with a two-month history of dysphagia, and was found on endoscopy to have a carcinoma of the oesophagus at 30 cm. Following biopsy, the lesion was dilated, and a 15 cm Celestin pulsion tube inserted. The patient obtained good relief from his dysphagia, and remained asymptomatic for seven months. He then complained of further dysphagia and arrangements were made for a barium swallow. The following day, however, he returned because of epigastric pain, and was admitted to hospital. Examination revealed vague epigastric tenderness, but there were no other abdominal signs. A barium study was performed, and showed the Celestin tube to have migrated to the stomach; but the radiopaque marker on a separated fragment of the tube, lying in the right iliac fossa, was not noted (Fig. 2). Elective surgical removal of the tube from the stomach was therefore planned, but the night before the operation the patient's condition deteriorated suddenly. He became profoundly shocked and died.

A post-mortem examination revealed that the Celestin tube had fractured, and the distal fragment was found to have lodged in the mid-part of the small bowel. The proximal bowel was dilated and engorged with full thickness necrosis of the wall, which perforated on handling. The damage to its wall had resulted from the "cheese-wire" effect of the uncoiled nylon spiral connecting the two parts of the tube.

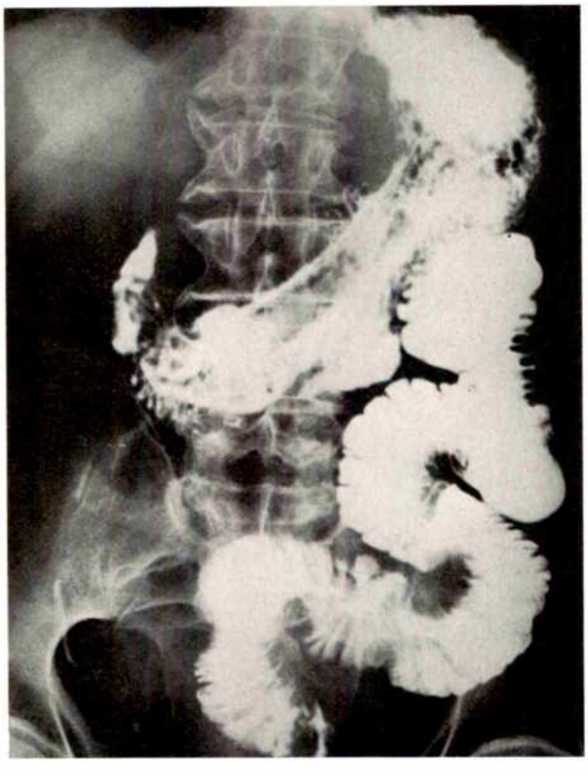


Fig. 2.

Main body of fractured tube in stomach. Distal separated fragment lying in right iliac fossa.

Discussion

The importance of radiological monitoring at the time of insertion of a Celestin tube is well known. The image intensifier is used to screen pulsion tubes into place, and plain radiographs are essential soon afterwards to check the position of the tube. Lateral views are the most satisfactory for this purpose. Following this, regular monitoring is recommended, with a major clinical and radiological review after six months. Following intubation for benign strictures, Ranson and John (1979) have suggested that the tube should be removed after this length of time, and replaced at a later date if necessary.

Most Celestin tubes incorporate simply a linear radiopaque marker in the shaft and in the distal flange (Fig. 3A). The two separated portions of this marker can be seen on an abdominal X ray following breakage of the tube. In some projections, the shaft and flange marker lines are seen to meet in a V-shape, but when these two parts of marker are superimposed, they will present simply as a single radiopaque line (Fig. 3B). When the separated distal fragment is short, therefore, it may present only as a short single line while the proximal part of the tube can easily be mistaken as normal in length.

The small size of such a distal fragment renders the implications of tube fragment no less serious, and the need for awareness of this complication is therefore emphasized.

In follow-up radiography after a Celestin tube insertion, not only should its position be checked but also its integrity. If the radiopaque marker is unbroken and the flange is clearly seen then the tube is intact. More than one projection may be needed to show this, although it is probably simpler to rotate the patient under fluoroscopy.

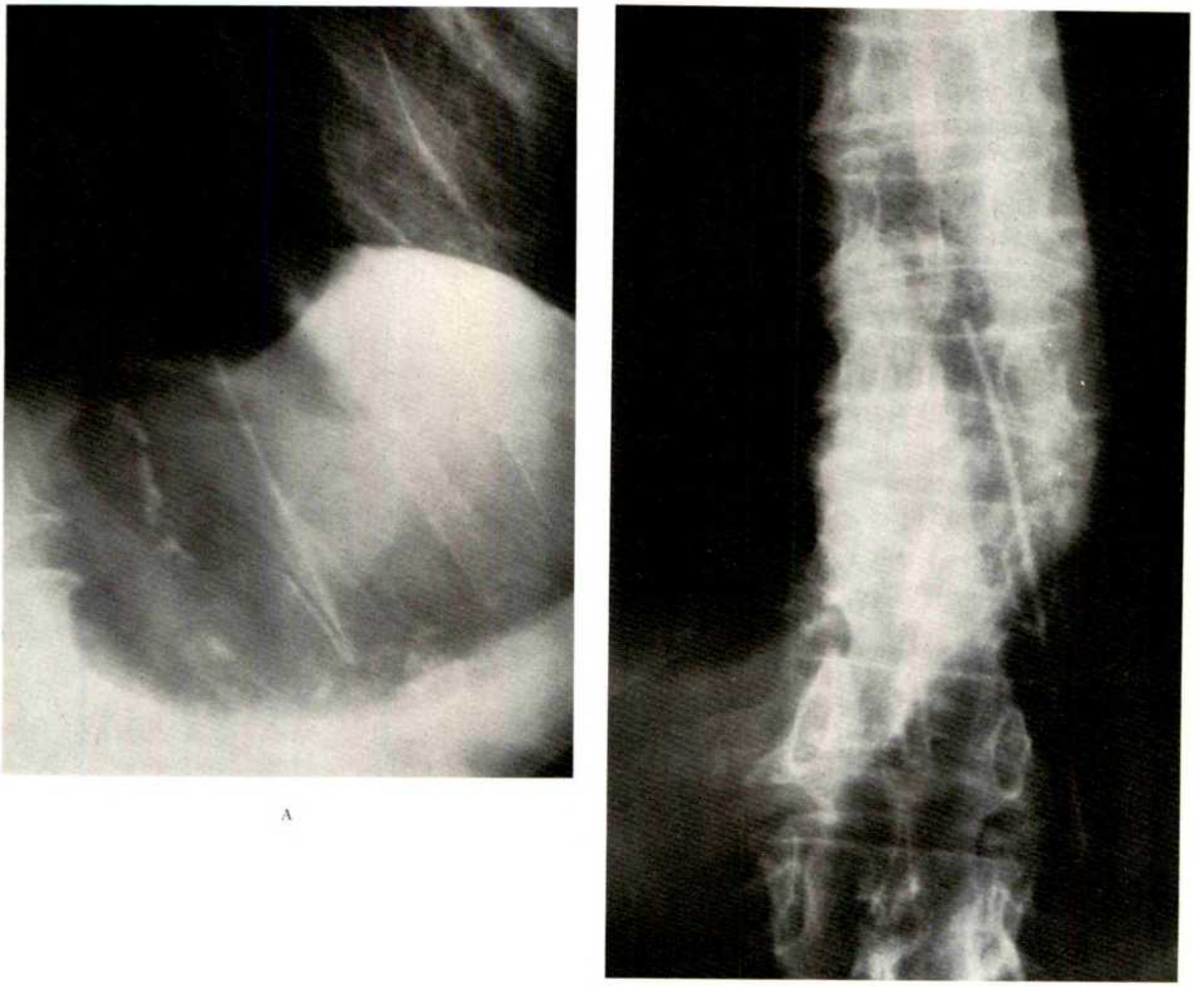


FIG. 3.

(A) Celestin tube identified by radiopaque marker showing main body of tube and flange intact.
(B) With different projection flange not seen.

If there is any suspicion whatever that the tube may have fractured then a radiograph of the whole abdomen is essential to search for a distal fragment. The main body of the tube may either remain in the oesophagus or move, as in this case. If a separated fragment is seen on abdominal X ray, operative intervention is a matter of urgency. Either laparotomy may be performed and the fragments removed, or the nylon joining tube fragments may be divided endoscopically. The proximal fragment may then be retrieved, and the distal one left to pass through the bowel.

Recent modifications have been made in the design of Celestin tubes, aimed at reducing the risks of fragmentation. Activators have been added to the latex which render it more resistant to structural deterioration, while leaving it otherwise unchanged. Tubes have also been produced with separate coils of nylon, so that there is no long spiral to uncoil and cause pressure necrosis, should a fracture occur.

Although these modifications are likely to reduce the number of complications encountered, they do not diminish the need for awareness and early radiological diagnosis of these serious problems.

ACKNOWLEDGMENT

We are indebted to Mr. L. R. Celestin for his helpful advice during the preparation of this article.

REFERENCES

BROWN, P. and HUGHES, R. G., 1979. Late complications of endoscopic oesophageal tube insertion. *British Medical Journal*, *ii*, 970–971.

1981, *British Journal of Radiology*, *54*, 1000–1001

CELESTIN, L. R., 1959. Permanent intubation in inoperable cancer of the oesophagus and cardia. *Annals of the Royal College of Surgeons of England*, *25*, 165–170.

1978. New techniques for intubation of the Celestin pulsion tube. *4th World Congress of Digestive Endoscopy, Madrid, 1978*, Abstracts, p. 97.

LAUGHLIN, E. H. and WALKER, W. Y., 1980. Fragmentation of Celestin tube. A cause of fatal intestinal perforation. *Journal of Thoracic and Cadiovascular Surgery*, *80*, 17–20.

MACGOWAN, K. M., 1980. Celestin tube disruption. *British Journal of Surgery*, *67*, 421–424.

MACKENZIE, I., WHYTE, A. S. and TARKEL, H. I., 1976. Structural deterioration in Celestin tubes. *British Journal of Surgery*, *63*, 851–852.

MEYER, W. and ZANNIT, A., 1980. Multiple Dünndarmperforationen nach Oesophagus-endoprosthesen-implantationen. *Der Chirurg*, *51*, 659–660.

RANSON, M. B. and JOHN, H. T., 1979. Complications associated with the use of the Celestin tube for benign oesophageal obstruction. *British Journal of Surgery*, *66*, 110–112.

RAO, D. D., 1978. Celestin intubation of the oesophagus. *Journal of the Royal College of Surgeons of Edinburgh*, *23*, 98–99.

SHAW, J. F. L. and COOMBES, G. B., 1979. Multiple intestinal perforations due to Celestin tube. *British Journal of Surgery*, 66, 807–808.

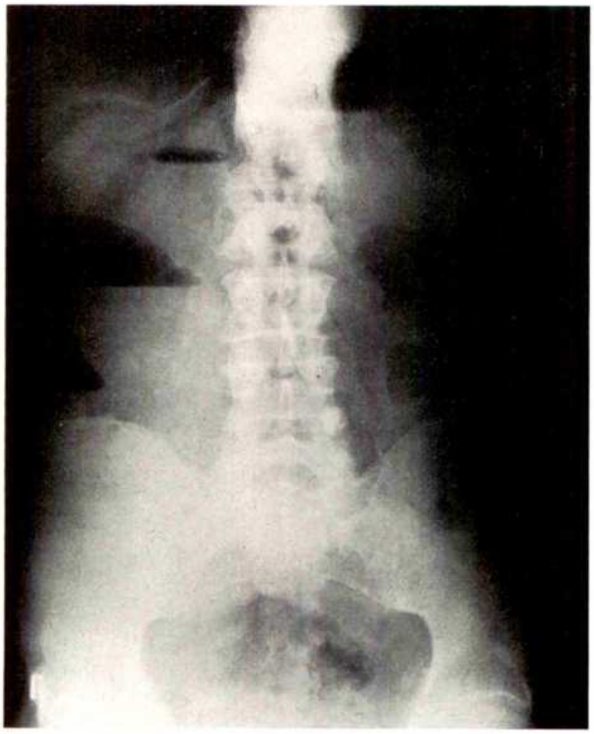
Recurrent gall-stone ileus

By A. U. Haq, A. H. Morris and H. Daintith

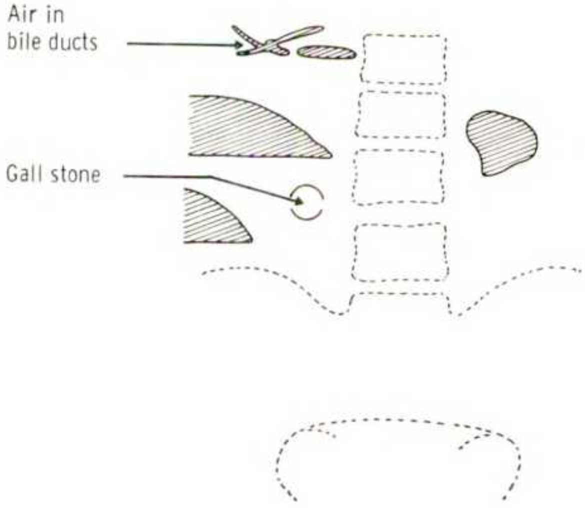
Department of Radiology, City Hospital, Nottingham

(*Received November 1980 and in revised form April 1981*)

Only two cases of recurrent gall-stone ileus diagnosed in the post-operative period have been reported. Guistra *et al.* (1977) reported the only fully described case. Eisenman *et al.* (1967) used the radiographs of a case in a review of radiographic signs in gall-stone ileus. In both, the diagnosis could have been made on a plain abdominal radiograph. We report a case in which plain films were inadequate for diagnosis.



A



B

FIG. 1.

CASE REPORT

A 73-year-old man was admitted with a day's history of vomiting and colicky, right iliac fossa pain. He had diffuse right-sided abdominal tenderness with maximal tenderness in the iliac fossa.

The plain abdomen radiographs (Fig. 1) showed air in the biliary tree, multiple dilated jejunal loops with fluid levels on the right side and a faint ring calcification to the right of the spine. The appearances were those of a gall-stone ileus.

At laparotomy, a gall-stone was seen impacted one metre from the ileo-caecal valve with proximal small bowel dilatation. The mucosa at the site of impaction was viable. The

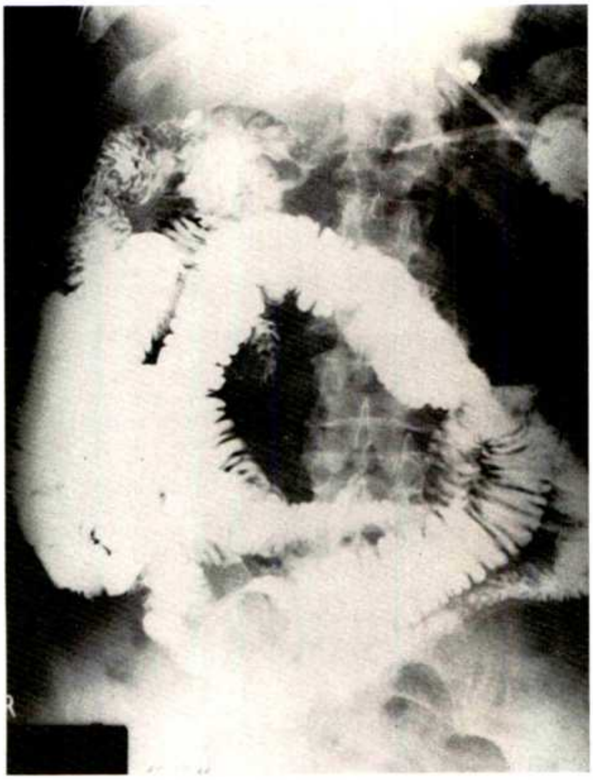


FIG. 2.

stone was milked back and removed via a jejunotomy. There were multiple adhesions in the region of the gall bladder and this was not explored. On the ninth post-operative day he had a rigor and on the following day the abdominal wound discharged small bowel contents.

A sinogram showed that the skin opening communicated with a large abscess cavity but no small bowel connection was demonstrated. Dilated small bowel loops indistinguishable from those seen in localized peritonitis were seen.

250 ml of barium suspension were injected through a nasogastric tube to outline the small bowel. There was dilatation of the jejunum with a maximum diameter of 6 cm and well-preserved valvulae conniventes (Fig. 2). A large filling defect due to a noncalcified gall-stone was seen in the distal jejunum. The small bowel beyond the gall-stone was normal. Because the patient was a poor anaesthetic risk and the obstruction was not complete surgery was delayed. A week later he developed severe abdominal pain with distention and rigidity and laparotomy was performed as a life-saving procedure.

The proximal small bowel was dilated, the jejunotomy had broken down and a gall-stone was impacted 0.75 m distal to it. The gall-stone was removed, the previous jejunotomy site resutured and the abdomen closed. After a stormy post-operative period the patient made a good recovery.

DISCUSSION

The radiological criteria for the diagnosis of gall-stone ileus are well established (Rigler *et al.*, 1941; Raf and Spongen, 1971; Day and Marks, 1975). They are: partial or complete obstruction; contrast medium or air seen in the biliary tree in 30–40% of cases; and a previously observed gall-stone may be seen to have moved (probably this sign is seen in not more than 10% of cases). There may be little gas and few fluid levels as the small bowel may be distended with liquid so that bowel loops are seen in the plain abdomen film without effacement of the valvulae conniventes. This pattern is seen in nearly 90% of cases (Eisenman *et al.*, 1976).

A positive preoperative diagnosis of gall-stone ileus is only possible on plain films if the gall-stone is calcified but 70% of gall-stones are nonopaque. In our case only a thin ring of calcification was present in the gall-stone removed at the first operation and while the ring calcification was visible on the film it has not reproduced well in the print (Fig. 1). This should perhaps have alerted the surgeons to the possibility of further noncalcified stones as solitary gall-stones are infrequent. The diagnosis of gall-stone ileus in the post-operative period is so difficult that contrast studies are essential if a correct diagnosis is to be made before the second laparotomy.

It has been thought that an incomplete obstruction could be converted to a complete one by impaction of barium. This was shown not to be so by Nelson *et al.* (1963) and the usefulness of small bowel barium studies in obstruction was stressed by Miller and Folke (1969) in a study of 225 cases.

ACKNOWLEDGMENTS

We thank Dr. Peter Davies for his help and advice, Miss Sue Chamberlain who typed the manuscript and the radiographers at the City Hospital, Nottingham.

REFERENCES

DAY, E. A. and MARKS, C., 1975. Gall-stone ileus: A review of the literature and presentation of 34 new cases. *American Journal of Surgery*, *129*, 552–558.

EISENMAN J. I., FINCK, E. J. and O'LOUGHLIN, B. J., 1967. Gall-stone ileus: a review of roentgenographic findings and a report of a new roentgen sign. *American Journal of Roentgenology*, *101*, 361–366.

GUISTRA, P. E., ROOT, J. A. and KILLORAN, P. J., 1977. "Gall-stone ileus" times two. *American Journal of Gastroenterology*, *67*, 613–615.

MILLER, R. E. and FOLKE, B., 1969. Large amounts of orally administered barium for obstruction of the small intestine. *Surgery, Gynaecology and Obstetrics*, *129*, 1185–1188.

NELSON, S. W., CHRISTOFORIDIS, A. J. and ROENICK, W. J., 1963. Barium suspension versus watersoluble compounds in the study of obstruction of the small bowel. *Radiology*, *8*, 252–254.

RAF, L. and SPONGEN, L., 1971. Gall-stone ileus. *Acta Chirurgica Scandinavica*, *137*, 665–675.

RIGLER, L. G., BORMAN, C. N. and NOBLE, J. F., 1941. Gall-stone obstruction: pathogenesis and roentgenographic manifestations. *Journal of the American Medical Association*, *117*, 1753–1159.

1981, *British Journal of Radiology*, *54*, 1002–1004

Case reports

Osteoblastic metastases in renal cell carcinoma

By *A. I. Neugut, M.D., Ph.D., *E. S. Casper, M.D., †T. A. Godwin, M.D. and ‡Julius Smith, M.D., M.R.C.P., F.R.C.R.

Departments of *Medicine, †Pathology and ‡Radiology, Memorial Sloan-Kettering Cancer Center, Cornell University Medical College, New York, New York 10021, USA

(*Received June 1981*)

Renal cell carcinoma (hypernephroma, renal adenocarcinoma) metastasizes to the skeleton in approximately 10% of cases and characteristically produces expansile lytic lesions (Forbes *et al.*, 1977). Although sclerotic changes may be seen following radiotherapy, osteosclerotic metastases in this condition prior to therapy are virtually unknown (Forbes *et al.*, 1977; Sherman and Pearson, 1948). We report here a well-documented case of renal cell carcinoma which produced osteoblastic metastases and was confirmed by autopsy examination.

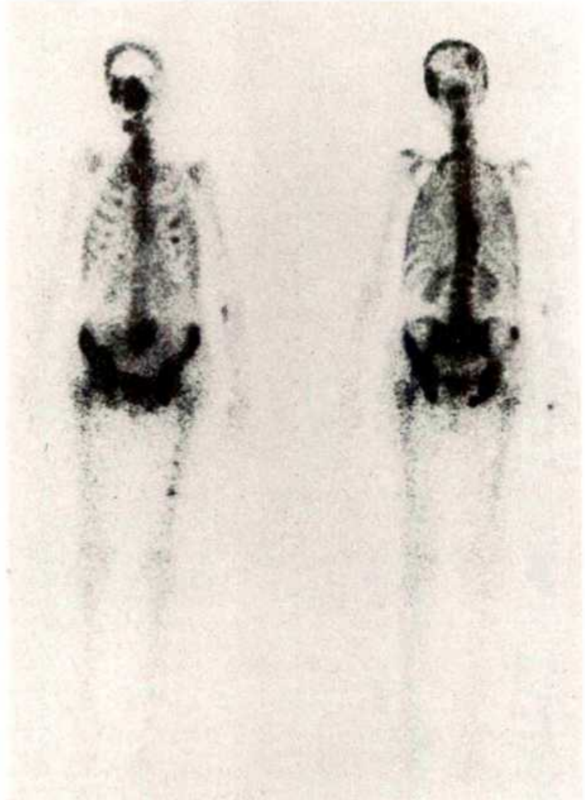


FIG. 1.
Bone scan showing widespread skeletal metastases.

CASE REPORT

A 68-year-old white female presented to a local hospital with a one-month history of headaches and diplopia in October 1979. Evaluation revealed the presence of a pituitary tumour. The patient underwent trans-sphenoidal hypophysectomy which revealed metastatic papillary adenocarcinoma. A search for the primary lesion and an evaluation for the extent of disease included an upper GI series, barium enema, mammography and liver-spleen scan which were all normal, but ultrasonography of the abdomen showed a right intrarenal mass. The patient was treated with steroids and discharged for further study as an outpatient. During the period of this evaluation, she became hypotensive and developed severe nausea and vomiting. The patient was brought to the Memorial Sloan-Kettering Cancer Center where she responded to treatment for adrenal crisis. CT of the abdomen revealed a large mass in the right kidney consistent with a renal cell carcinoma. A bone scan (Fig. 1) showed widespread skeletal metastases, and radiographs demonstrated osteoblastic metastases in the sella turcica right femur, spine and pelvis (Figs. 2, 3). In May 1980 the patient was treated with radiation to the sella turcica and the symptomatic right femur and hemi-pelvis. Following radiotherapy, the patient received aclacinomycin-A, an anthracycline antineoplastic agent (Casper *et al.*, 1981). She became septic during the period of drug-induced pancytopenia and, in spite of antibiotics and supportive treatments, died.

Pathology

Post-mortem examination disclosed a 7×6.5×4 cm tumour in the lower pole of the right kidney. The tumour

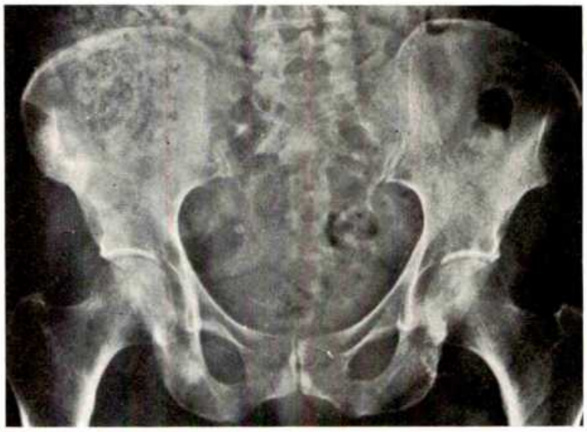


FIG. 2.
Radiograph of the pelvis demonstrating multiple osteoblastic metastases.

Address for reprints: Julius Smith, M.D., Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, New York 10021, USA.

was well circumscribed with compression of the adjacent renal parenchyma. There was fixation to the overlying renal capsule but no infiltration of the capsule, the renal pelvis or the renal vessels. The cut surface was homogeneously tan-brown and soft. Microscopically, the tumour was uniformly composed of well-differentiated small tubules lined by small cuboidal cells with minimal anaplasia (Fig. 3). Mucicarmine, Grimelius and Fontana stains were negative. These findings confirmed the presence of a primary well-differentiated renal cell carcinoma.

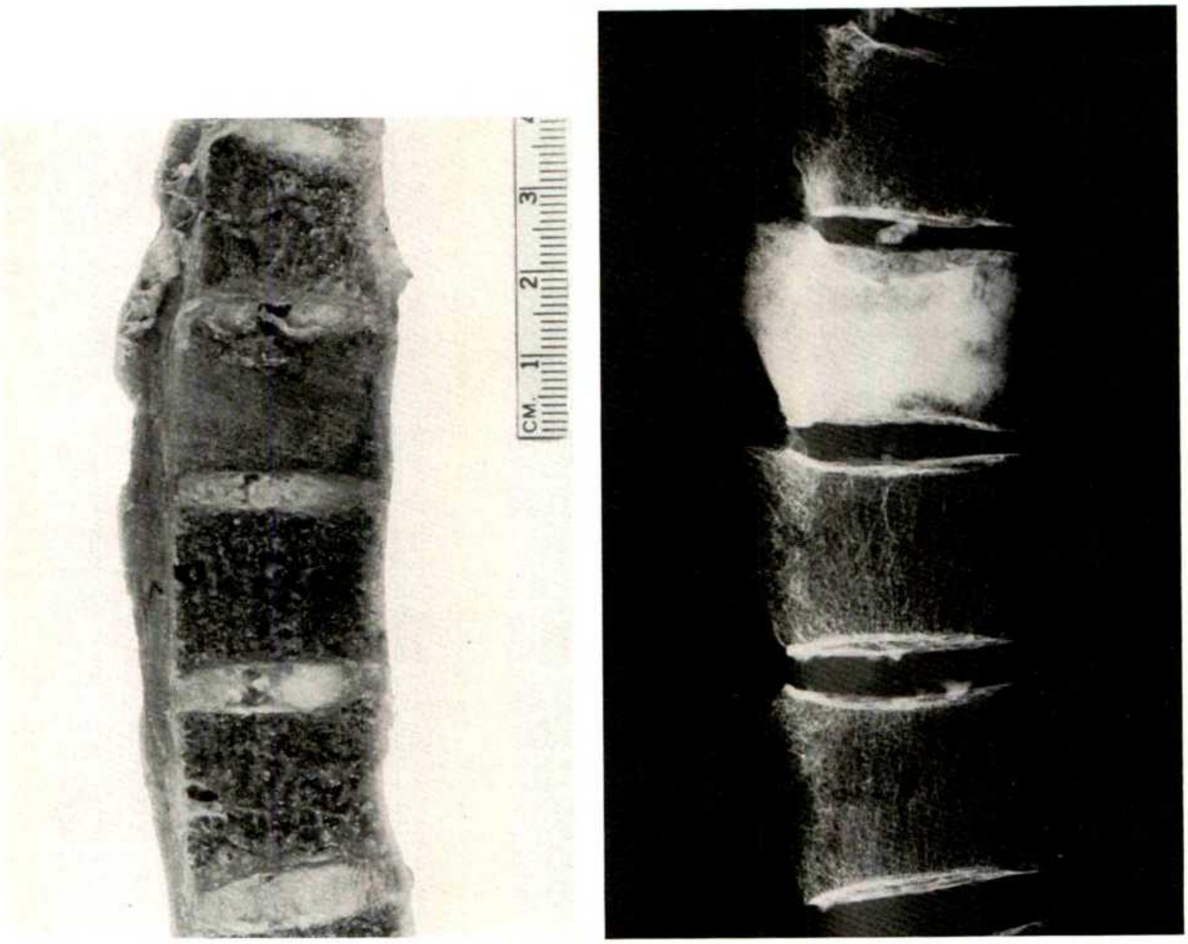
Several upper thoracic and cervical vertebrae were partially replaced by hard whitish tissue. Microscopically, there was well-differentiated adenocarcinoma intermingled with sclerotic bone.

A search for other primary malignant tumours, including careful examination of the breasts, gastrointestinal tract, pancreas and ovaries was negative.

DISCUSSION

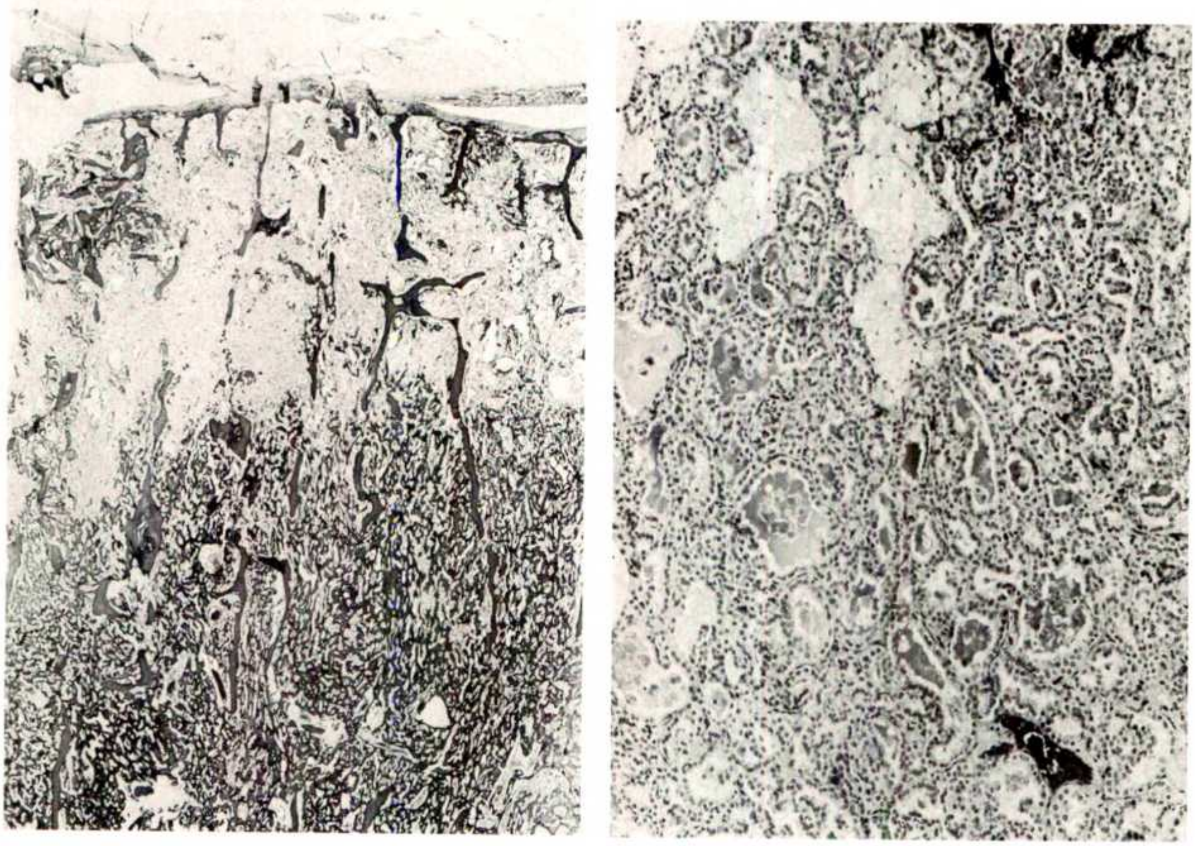
In a review of the literature, we were able to identify only one previous case of osteoblastic metastases from a primary renal cancer. Reidy (1975) reported a case of extensive osteoblastic metastases from a hypernephroma in a 34-year-old man. Unfortunately, autopsy confirmation was not obtained.

In general, purely osteoblastic metastases are much less common than purely osteolytic or mixed osteolytic and osteoblastic metastases. They are, therefore, a useful finding since the differential diagnosis is relatively limited. The majority of osteoblastic metastases is caused by prostate or breast cancer. Lymphoma is another well-known cause. Osteoblastic metastases may occur in patients with adenocarcinoma of the lung, but may occur in small-cell lung cancer as well (Napoli *et al.*, 1973). Osteoblastic metastases in carcinoid and mucin-secreting tumours of the gastrointestinal tract are rare but well-described. Medullary carcinoma of the thyroid is the only thyroid cancer to cause osteoblastic lesions (Milhaud *et al.*, 1969).



A FIG. 3. B

Post-mortem findings. (A) Upper thoracic vertebral sclerotic metastasis. (B) Radiodense lesion on specimen X ray.



C FIG. 3. D

(C) Low power micrograph of the sclerotic metastasis. (D) Well-differentiated adenocarcinoma in the kidney.

It is possible that osteoblastic metastases from renal cell carcinoma are not so rare as our review of the literature would suggest. As recently as 1959, osteosclerosis was felt to be incompatible with the diagnosis of myeloma (Murray and Haddad, 1959), but this presentation is now well recognized by radiologists and clinicians. The same situation may apply to renal cell carcinoma.

Renal cell carcinoma is noted for presenting in unusual ways, frequently by its humoral effects or with unusual metastases. This is the second reported case of renal cell carcinoma with osteoblastic metastases, but the first with pathological documentation. Renal cell carcinoma is a rare but possible cause of osteoblastic lesions and further cases deserve to be reported.

ACKNOWLEDGMENTS

The authors wish to thank Ms. Polly Hodge for her excellent secretarial assistance. Dr. Neugut is a Clinical Fellow of the American Cancer Society and is supported in part by a Clinical Cancer Education Program Grant No. CA 20449–05. Dr. Casper is the recipient of an American Cancer Society Junior Faculty Fellowship.

REFERENCES

CASPER, E. S., GRALLA, R. J. and YOUNG, C. W., 1981. Clinical phase I study of aclacinomycin A by evaluation of in intermittent intravenous administration schedule. *Cancer Research*, *41*, 2417–2420.

FORBES, G. S., MCLEOD, R. A. and HATTERY, R. R. 1977. Radiologic manifestations of bone metastases from renal carcinoma. *Americal Journal of Roentgenology*, *129*, 61–66.

MILHAUD, G., COUTRIS, G. and TUBIANA, M., 1969. Le cancer médullaire de la thyroide et le syndrome d'hyperthyrocalcitonine. *Presse Medicale*, *77*, 2129–2132.

MURRAY, R. O. and HADDAD, F., 1959. Hydatid disease of the spine. *Journal of Bone and Joint Surgery*, *41B*, 499–506.

NAPOLI, L. D., HANSEN, H. H., MUGGIA, F. M. and TWIGG, H. L., 1973. The incidence of osseous involvement in lung cancer, with special reference to the development of osteoblastic changes. *Radiology*, *108*, 17–21.

REIDY, J. F., 1975. Osteoblastic metastases from a hypernephroma. *British Journal of Radiology*, *48*, 225–227.

SHERMAN, R. S. and PEARSON, T. A., 1948. The roentgenographic appearance of renal cell cancer metastases in bone. *Cancer*, *1*, 276–285.

1981, *British Journal of Radiology*, *54*, 1005

November 1981

Case reports

Second primary neoplasm in a dysgerminoma patient

By *O. M. Koriech, F.R.C.R.

Regional Radiotherapy Centres, Newcastle General Hospital and Royal Victoria Infirmary, Newcastle upon Tyne

and G. H. D. McNaught, V.R.D., F.R.C.S.Ed.

Hartlepool General Hospital, Hartlepool, Cleveland

(*Received June 1981*)

Dysgerminoma is a rare germ-cell tumour of the ovary. Like its testicular counterpart, it is very radiosensitive; in the absence of any other germ-cell elements, dysgerminoma reponds well to radiation therapy. A cure rate of over 80% has been reported (Freel *et al.*, 1979).

Our case developed carcinoma of the pelvic colon at the age of 29 years, following the treatment of dysgerminoma 15 years previously.

Case Report

A 14-year-old girl presented in January 1966 with a 4½-month history of lower abdominal pain and swelling. A large pelvis-abdominal mass extending to the level of the umbilicus was found on examination. Laparotomy revealed an inoperable hard tumour arising from the pelvis and occupying the lower threequarters of the abdominal cavity. Debulking was then carried out. Histology revealed a florid neoplasm with irregular sheets and confluent mitoses diagnostic of dysgerminoma of the ovary. A course of radiotherapy to the pelvis and lower abdomen using megavoltage irradiation to a dose of 42 Gy (4200 rad) in 30 days was given. The patient remained well until July 1971 when she noticed a swelling in the epigastrium. The liver was enlarged and irregular and a space-occupying lesion was found on radioisotope scan. Further radiotherapy to the liver and epigastrium to a dose of 34 Gy (3400 rad) in 31 days caused complete disappearance of the clinical disease.

In December 1980, the patient developed subacute intestinal obstruction and laparotomy showed a small ring carcinoma of the apex of the pelvic colon. The liver was healthy on inspection and palpation. Suction enterostomy of small and large bowel was required to permit a primary resection of the colon. Histology reported a well-differentiated papillary mucoid adenocarcinoma invading the pericolic adipose tissue. The patient is well and back at work in April 1981. CEA in December 1980 was less than 2 μg/l, in April 1981 4 μg/l.

Discussion

Although bowel cancer is the second most common cancer in the female, it is rare under the age of 30. Familial polyposis and ulcerative colitis predispose to its development at an early age but were not present here. Radiotherapy is known to induce malignancy of the thyroid, breast, skin, liver, bone, lungs and other sites (Hirohata, 1976). The development of bowel cancer in this patient at the age of 29, some 15 years after the treatment of an ovarian primary, raises the possibility that this is a radiation-induced carcinoma.

Alternatively, it is possible that patients cured of ovarian dysgerminoma are prone to develop a second primary carcinoma as an innate characteristic of the patient.

The findings in this case indicate that radiation oncologists and gynaecologists should be aware of the possible development of a second primary carcinoma in young patients cured of a previous primary dysgerminoma.

REFERENCES

Freel, J. H., Cassir, J. F., Pierce, Virginia K., Woodruff, J. and Lewis, J. L., 1979. Dysgerminoma of the ovary. *Cancer*, *43*, 789–805.

Hirohata, T., 1976. Radiation carcinogenesis. *Seminars in Oncology*, *3*, 25–34.

---

*Present address: Department of Oncology, Riyadh Military Hospital, P.O. Box 7897, Riyadh, Kingdom of Saudi Arabia.

1981, *British Journal of Radiology*, 54, 1006–1008

Short communication

Mechanism of misonidazole-linked cytotoxicity and altered radiation response: role of cellular thiols

By J. E. Biaglow, Ph.D., Marie E. Varnes, Ph.D.

Department of Radiology, Division of Radiation Biology, Case Western Reserve University, Cleveland, Ohio 44106

M. Astor, M.A. and E. J. Hall, D.Sc.

Radiological Research Laboratory, College of Physicians and Surgeons, New York 10032, USA

(*Received March 1981 and in revised form July 1981*)

The effectiveness of misonidazole as a hypoxic radiosensitizer of mammalian cells is increased by prolonged exposure of hypoxic cells to the drug. Increased radiosensitization occurs even after the cells are washed free of excess drug (Hall and Biaglow, 1977; Whitmore *et al.*, 1978; Varnes *et al.*, 1981). Hall *et al.* (1977) suggested and Biaglow *et al.* (1978) found that drug intermediates, produced during hypoxic incubation of cells with misonidazole, might react with endogenous non-protein thiols (NPSH). These thiols function to protect the cell against deleterious intermediates that could otherwise attack and modify critical macromolecules such as DNA, RNA and protein. This hypothesis is in agreement with the cytotoxic mechanisms proposed earlier for many different nitro compounds (Biaglow, 1981). With respect to the effects of preincubation with misonidazole on the radiation response, alterations in both NPSH and protein thiols (Varnes *et al.*, 1981) would be expected to alter the shoulder of the radiation response curve if hydrogen-donating species such as NPSH are involved in chemical repair of radiation damage (Chapman *et al.*, 1973) or if thiol-containing enzymes are necessary for biochemical repair of damaged macromolecules (Han *et al.*, 1976).

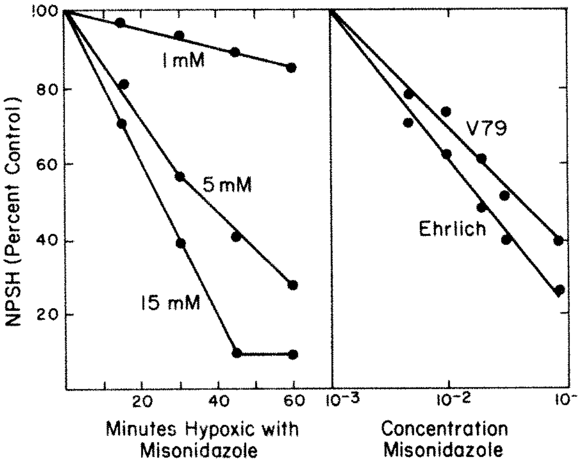
In addition to the role that endogenous thiols may play in inactivating toxic intermediates, it has been shown by Hall *et al.* (1977) that co-incubation of misonidazole with the thiol cysteamine prevents both the radiosensitization and the cytotoxicity of this drug. Chapman *et al.* (1973) had shown earlier that the radiosensitizing effects of nitro compounds could be reversed by cysteamine.

Several ensuing studies involving the mechanisms for the cytotoxic and radiosensitizing abilities of misonidazole have attempted to identify biochemical alterations produced by the drug and its metabolites. Varnes *et al.* (1981) demonstrated that misonidazole can react with both intracellular NPSH and with protein thiols. Loss of thiol was increased if glucose or ascorbate was present. Chapman *et al.* (1973), Watts *et al.* (1975), Harris *et al.* (1976; 1977) and Nygaard *et al.* (1980) found that the radiosensitizing effects of misonidazole were greater if NPSH were removed by diamide. On the other hand, Taylor and Rauth (1981) have found that exogenous cysteamine alters the profile of metabolites obtained from misonidazole-treated cells. Palcic *et al.* (1981) have shown that the hypoxic cytotoxicity of misonidazole can be modified in the presence of cysteamine and that the effect is pH dependent.

The above-mentioned studies suggest an important role for both endogenous NPSH as well as exogenous thiols in the radiosensitization and cytotoxic action of misonidazole. Therefore, we have continued our studies on the effects of misonidazole and of newly-developed hypoxic-cell radiosensitizers, in an attempt to (1) identify the alterations in the NPSH and (2) elucidate the role that the changes in NPSH play in cytotoxic and radiosensitizing effects of nitro compounds.

Figure 1A shows the effect of different concentrations of misonidazole on the NPSH of dense-cell suspensions of Ehrlich cells made hypoxic by their own metabolic consumption of oxygen. The cells were kept in suspension in a glass syringe by gentle rotation. The NPSH was determined by the Ellman method as modified by Varnes and Biaglow (1979). Thiol loss occurred at all drug concentrations. The effects of 15-minute incubations at different misonidazole concentrations on the thiol content of dense suspensions of hypoxic V79 and Ehrlich cells are seen in Fig. 1B. We have also measured the thiol content of the EMT6 tumour *in vivo*, five hours following a 1 mg/kg dose of misonidazole, and found no change in NPSH (data not shown).

In addition to misonidazole, the recently-developed nitroheterocyclic radiosensitizing compounds SR 2555 and



A FIG. 1. B

The effect of misonidazole on the non-protein thiol (NPSH) content of Ehrlich ascites tumour cells and V79 lung cells. Ehrlich cells were obtained from eight day tumour-bearing mice as previously described (Varnes and Biaglow, 1979). The cells were washed and resuspended at 0–4°C in 0.2 M HEPES-buffered physiological saline containing 0.01 M KCl, pH 7.4. V79 lung-cells grown as previously described were also suspended in the same buffered saline and at the same density (10^8/ml) as the Ehrlich cells. Cells were washed free of drug, and thiols determined (Varnes and Biaglow, 1979). (A) Ehrlich cells made hypoxic by their own metabolic consumption of oxygen for various times. (B) Fifteen-minute incubations of V79 and Ehrlich cells.

TABLE I

Effect of nitro compounds on thiol content and cytotoxicity of V79 lung cells

2 mM drug	Relative rate of reduction[1]	NPSH[2]	Surviving fraction[3]	Enhancement ratio[4]	Extra enhancement ratio due to preincubation[5]
SR 2555	0.28	0.43	0.50	2.1	—
SR 2508	0.65	0.36	0.30	2.1	1.0
Misonidazole	1.0	0.24	0.07	2.1	1.7

1. V79 cells were suspended in 0.05 M HEPES buffer pH 7.4 with 0.01M KCl and 0.15M NaCl with and without 5 mM drug. The rate of reduction of drug was determined by continuously monitoring peroxide production with cells incubated in the presence of 0.2 mM N-ethylmaleimide and 3 mM azide. Drug/misonidazole reduction 1 (0.0013 mM H_2O_2/min) (Schroy and Biaglow, 1981).
2. Thiol content was determined after 5 h hypoxic incubation with 2 mM drug in complete growth medium containing 10% calf serum buffered with 0.04 M HEPES, pH 7.4, 37°C.
3. The surviving fraction was determined after 5 h of hypoxic incubation in growth medium with 2 mM drug (Astor and Hall, 1981).
4. The enhancement ratio was determined under hypoxic conditions with 5 mM drug (Astor and Hall, 1981).
5. 10^6 cells were incubated at 37.5°C with a 2 mM concentration of the appropriate drug. The extra enhancement ratio is defined as the radiosensitivity of cells incubated with 2 mM drug for 5 h/radiosensitivity of cells incubated with 2 mM drug for 1 h.

SR 2508 (Brown and Lee, 1981) were also tested for their effects on the NPSH of hypoxic cells *in vitro* under conditions routinely used for our radiation and cytotoxic studies (Table I). Removal of thiol in complete growth medium containing serum was greatest for misonidazole, followed by SR 2508 and SR 2555. These drugs were found to be slightly more effective when incubated with hypoxic Ehrlich cells in phosphate buffered saline. In general, reduction of drug (see first column, Table I) as well as the depletion of thiols by SR 2555 and SR 2508 (second column) correlates with the hypoxic cytotoxicity (third column). The more metabolically-active misonidazole is the most toxic. The small fraction of hypoxic cells surviving the five hour misonidazole treatment was more sensitive to radiation than cells immediately exposed (see column 4). Similar effects occur with SR 2508 but require incubation times of seven hours or longer (data not shown).

In conclusion, our results suggest that continued studies on the relationship between cellular thiols and drug cytotoxicity as well as enhanced radiation response, *in vitro*, will lead to fruitful new information concerning the mechanism of action of these drugs. Our results with dense suspensions of cells (Fig. 1) indicate that relatively large drug concentrations for prolonged periods of time will be necessary to deplete tumour thiols *in vivo*. Additional work is necessary to determine if cytotoxic and radiation responses *in vivo* are related to drug-linked loss of thiol.

Acknowledgments

This investigation was supported by Contract DE-AC02-78EV04733 from the Department of Energy and Grant Nos. CA-13747, CA12536, CA18506 and CA13696 awarded by the National Cancer Institute, DHEW.

REFERENCES

Astor, M. and Hall, E. J., 1981. Newly synthesized hypoxia-mediated drugs as radiosensitizers and cytotoxic agents. Submitted to *International Journal of Radiation Oncology Biology Physics*.

Biaglow, J. E., 1981. Cellular electron transfer and radical mechanisms for drug metabolism, *Radiation Research* (in press).

Biaglow, J. E., Varnes, M. E. and Jacobson, B., 1978. The effect of nitro-heterocyclic cell radiosensitizing drugs on non-protein thiols of Ehrlich ascites cells, *Radiation Research*, *74*, 499.

Brown, J. M. and Lee, W. W., 1981. Pharmokinetic considerations in radiosensitizer development radiation sensitizers. In *Cancer Management*, *5*. Ed. by L. Brady, (Masson Press, New York), pp. 2–13.

Chapman, J. D., Reuvers, A. P., Borsa, J. and Greenstock, C. L., 1973. Chemical radioprotection and radiosensitization of mammalian cells growing *in vitro*, *Radiation Research*, *56*, 291–306.

Hall, E. J., Astor, M. and Biaglow, J. E., 1977. On the cytotoxicity of the hypoxic radiosensitizer Ro-07-0582 and the reversal of the cytotoxic effect with cysteamine, *British Journal of Cancer*, *35*, 809–815.

Hall, E. J. and Biaglow, J. E., 1977, Ro-07-0582 as a radiosensitizer and cytotoxic agent, *International Journal of Radiation Oncology Biology Physics*, *2*, 521–530.

Han, A., Sinclair, W. K. and Kimler, B. F., 1976. The effect of N-ethylmaleimide on the response to X-rays of synchronous HeLa cells, *Radiation Research*, *65*, 337–350.

Harris, J., Koch, C. J., Power, J. and Biaglow, J. E., 1977. Radiosensitization of hypoxic cells by diamide. II. Studies of mechanism, *Radiation Research*, *70*, 585–596.

Harris, J. W., Power, J. A. and Koch, C. J., 1976. Synergistic chemical radiosensitization of hypoxic mammalian cells, *International Journal of Radiation Oncology Biology Physics*, *1*, 487–489.

Nygaard, O. F., Biaglow, J. E. and Harris, J. W., 1980. Role of non-protein thiols in intracellular radiation response: biochemical studies with diamide. In *Cancer Management*, *5*. Ed. by L. Brady. (Masson Press, New York), pp. 164–170.

Palcic, B., Skov, K. A. and Skarsgard, L. D., 1981. Effect of reducing agents on misonidazole cytotoxicity. In *Cancer Management*, *5*. Ed. by L. Brady. (Masson Press, N.Y.) pp. 436–437.

Schroy, C. B. and Biaglow, J. E., 1981. A novel use of an oxidase electrode to determine factors influencing the *in vitro* production of hydrogen peroxide by Ehrlich cells and 1-chloro-2, 4-dinitrobenzene, submitted to *Biochemical Pharmacology*.

Taylor, Y. C. and Rauth, A. N., 1981. The effects of ascorbate, cysteamine, reduced glutathione, MTDQ and O_2 on the toxicity and metabolism of misonidazole. In *Cancer Management*, *5*. Ed. by L. Brady. (Masson Press, New York).

Varnes, M. E. and Biaglow, J. E., 1979. The reaction of the carcinogen 4-nitroquinoline-1-oxide with non-protein thiols of mammalian cells, *Cancer Research*, *39*, 2960–2970.

VARNES, M. E., BIAGLOW, J. E., HALL, E. J. and KOCH, C. J., 1981. Depletion of non-protein thiols of hypoxic cells by misonidazole and metronidazole: implications for cytotoxicity. In *Cancer Management, 5.* Ed. by L. Brady. (Masson Press, New York), pp. 121–126.

WATTS, M. E. WHILLANS, D. W. and ADAMS, G. E., 1975. Studies on the mechanisms of radiosensitization of bacterial and mammalian cells by diamide, *International Journal of Radiation Biology, 27,* 259–267.

WHITMORE, G. F., GULYAS, S. and VARGHESE, A. J., 1978. Sensitizing and toxicity properties of misonidazole and its derivatives, *British Journal of Cancer, 37, Supplement III,* 115–119.

Book reviews

Clinics in Diagnostic Ultrasound. 4. Two-dimensional Echocardiography. Ed. by Joseph A. Kisslo, pp. 204 + 111 Figs. + 3 Tables, 1980 (Churchill Livingstone, New York/Edinburgh/London), £11·00.
ISBN 0–443–08076–3

The series "Clinics in Diagnostic Ultrasound" is produced under a general Editorial Board, and this volume is edited by Dr. J. A. Kisslo, Assistant Professor of Radiology and Director of the Clinical Cardiac Laboratory, Duke University, South Carolina, with papers by 28 distinguished contributors.

In the first chapter a short history of echocardiography is given. Emphasis is then made on placing echocardiography in perspective with all the other non-invasive and invasive cardiological investigative techniques which allow the physician to define the anatomical changes in the diseased heart and their severity, the physiological consequences of these changes, the aetiology of the condition and its prognosis. It is stressed that as most patients with heart disease have a chronic condition, there is a challenge to develop and explore the relative usefulness of non-invasive procedures compared with less desirable invasive procedures in order to follow the course of cardiac disease and its response to treatment. The importance of ensuring that very close cooperation exists in the future between specialists in radiology, cardiology, surgery, paediatrics, bio-engineering and computer science is stressed also. In this environment echocardiography will benefit from a collaborative effort. The next chapter deals with measurement of M-mode echocardiography and it defines and assesses the various endpoints defined by the M-mode Standards Committee of the American Society of Echocardiography. This is a very useful chapter.

The following chapter examines the variables that are capable of influencing echocardiographic measurements, such as the position of the patient, transducer position and physiological variables which must be taken into account when interpreting ultrasonic data. The next chapter describes the various ultrasonic two-dimensional echocardiographic methods available, including the recommended examination technique, and defining also current nomenclature for transducer location. There follow chapters on the echocardiographic diagnosis of mitral valve disease, assessment of left ventricular outflow obstruction, vegetative endocarditis, evaluation of the left ventricle by two-dimensional echocardiography, left ventricular hypertrophy, detection of intracardiac masses by cross-sectional echocardiography, pericardial effusion, echocardiographic comparisons to standard radiographic methods and finally contrast two-dimensional echocardiography. As relevant in these chapters, the M-mole echocardiography findings are described and their limitations assessed. The additional contribution that two-dimensional echocardiography can make to the assessment of the condition is given in some detail. The text is clear and the illustrations are remarkably good in spite of so many being real-time. An excellent feature of this volume is the well chosen bibliography for each chapter. The book ends with five mind-stimulating case studies.

This book is excellent value. It should be in every radiology and cardiac department in which echocardiography is practised and also in every teaching centre.

F. G. M. ROSS.

Clinics in Diagnostic Ultrasound. 5. New Techniques and Instrumentation in Ultrasonography. Ed. by P. N. T. Wells and M. C. Ziskin, pp. 245, 1980 (Churchill Livingstone, New York/Edinburgh/London), £12·00.
ISBN 0–443–08075–5

If a prize were to be given for the most valuable innovation in medical imaging in the twentieth century, ultrasound would be a strong contender just on present performance, and will be stronger still when a variety of current new ideas have had time to bear fruit. This volume on new techniques, edited by two leading figures in the field, should therefore be very welcome. It contains 14 chapters, all by different authors, on topics ranging from ultrasonic computerized tomography to routine preventive maintenance and, it must be said, has the unevenness of approach and quality that so often characterizes a multi-author volume.

It is difficult to know at what kind of audience the authors are aiming. Taken literally, the series title "Clinics . . ." seems to imply a practical, bedside teaching approach but the most successful chapters here are rather more in the style of essays suitable for arm-chair reading. The chapters on transmission imaging, Doppler ultrasound, tissue characterization and, perhaps, acoustic microscopy will be good reading for most radiologists and physicists, and that on real-time scanning systems will be valuable for those who have not already encountered the material elsewhere. Many of the other chapters however are disappointing: one has the feeling in places that this was an extra bit of writing that the author agreed to take on but then regretted and could only come up with a pot boiler. The final chapter, entitled "A Glossary for Diagnostic Ultrasound Instrumentation", is a worthy attempt to get us all to say what we really mean, but the author still has a good deal of homework to do—on "acoustic impedance", "beam width", "coherent" and "confocal", just for a start.

All in all another curate's egg: excellent in parts.

C. R. HILL.

1981, *British Journal of Radiology*, *54*, 1009–1010 NOVEMBER 1981

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Preset counts or preset time?

THE EDITOR—SIR,

In a recent article in this Journal (Constable and Cranage, 1981), the problem of recognizing the superscan in prostatic bone scintigraphy was reviewed. In Fig. 1 and Fig. 2 of that article a normal scan and a superscan were displayed. We were somewhat concerned to observe the superscan having, on average, a lower film density than the normal scan. Osmond *et al.* (1975) describe the superscan as producing "a marked increase in bone radionuclide concentration" and it therefore should display a higher overall film density than a normal bone scan. For comparison we show a normal bone scan (Fig. 1) and a superscan (Fig. 2) as produced by a similar procedure to that described by Constable and Cranage. The superscan is immediately recognized by the large increase in film density over the skeletal areas. A policy of imaging for preset time is adopted within this department and we wonder if the relatively low film density shown in Constable's article may be due to preset-count imaging. The superscan is made self-evident with the use of preset-time imaging without using a computer system for acquisition, storage and region-of-interest processing of the scan.

The policy of preset-time imaging is adopted to try and present to the eye of the observer some quantitative information in a readily appreciable manner. A low overall film density represents a poor uptake of radiopharmaceutical and a high overall film density represents a high uptake. If the images are outside the linear portion of the film's grey-scale response, then repeat imaging or, if the images have been digitized and stored, repeat display of the images is used to show the finer details of the scan. However, this is not undertaken until the gross diagnostic feature of high or low uptake has been demonstrated.

If imaging procedures are undertaken using preset counts, a note of the count rate must be made and this together with the relative uptake within the scan used to assess if high or low uptake is present within the scan. This would appear to put an unnecessary burden on the observer for little or no return.

Another example of the advantage of preset-time imaging is in lung-perfusion scanning of patients where the views are severely limited, for example in the ITU patient. If preset counts or preset information density is used for the two lateral views these may look very similar even in the patient with absent perfusion in one lung. Of course the anterior, posterior or oblique views would highlight asymmetries in

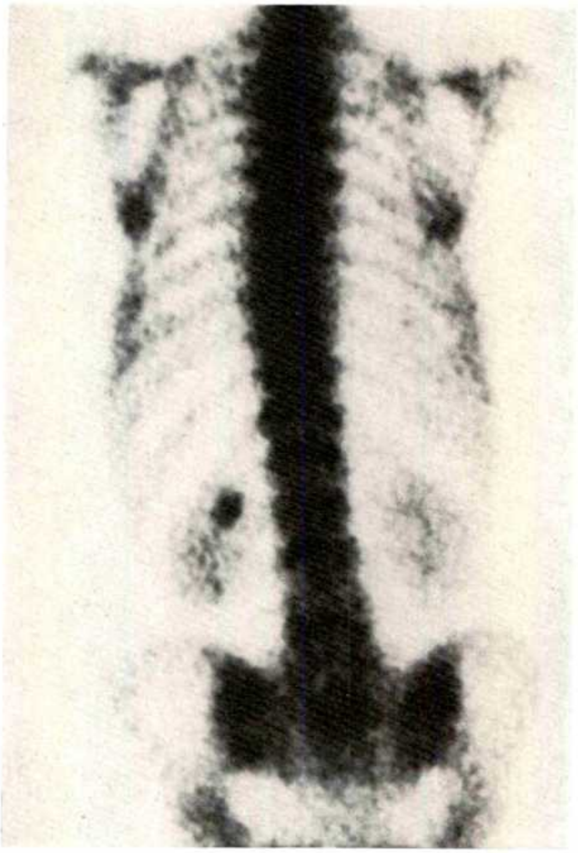


FIG. 1.

A normal bone scan using preset time.

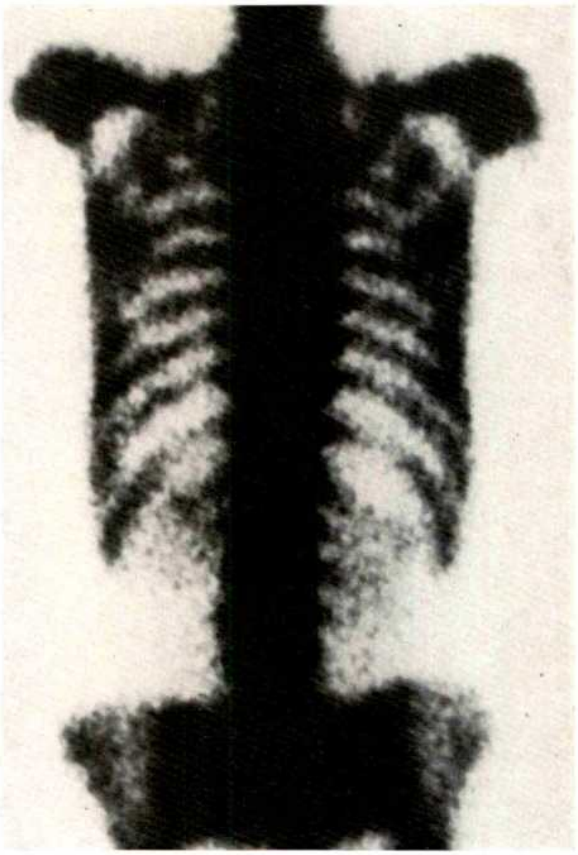


FIG. 2.

A superscan using preset time.

the usual case but if these views were not possible a grossly abnormal scan could be presented as normal.

Whilst accepting that some adjustment for changes in organ size is necessary to produce a low repeat imaging rate, we have found in practice that an adjustment for body weight or organ size maintains the repeat imaging rate at a negligible level. No system will give perfect grey-scale representation of all nuclear-medicine images but the use of preset-time imaging does at least give a first order presentation of organ uptake.

Yours, etc.,
C. P. Wells,
F. M. Hall,
P. J. Mountford,
A. J. Coakley.

Kent and Canterbury Hospital,
Canterbury CT1 3NG.
(*Received April 1981 and in revised form August 1981*)

REFERENCES

Constable, A. R. and Cranage, R. W., 1981. Recognition of the superscan in prostatic bone scintigraphy. *British Journal of Radiology*, *54*, 122–125.

Osmond, J. D., Pendergrass, H. P. and Potsaid, M. S., 1975. Accuracy of ^{99m}Tc-diphosphonate bone scans and roentgenograms in the detection of prostate, breast and lung carcinoma metastases. *American Journal of Roentgenology*, *125*, 972–977.

(*Authors' reply*)

The Editor—Sir,

We are grateful to C. P. Wells and his colleagues for pointing out the well-known difficulties of visually assessing gamma-camera scans and largely agree with their preset-time method for partly overcoming them.

We always apply the preset-time method when studying a given patient but have been less successful in applying it more generally owing to the wide range of picture quality thereby achieved.

Scans from many sources often have to be evaluated and compared without sufficient knowledge of the conditions under which they were obtained. The use of simple quantitative indices, such as our own "T12" index, can be most helpful in avoiding misinterpretation even when a superscan image is less intense than a normal scan as illustrated in our paper.

It would be of interest to hear other people's views on the preset-time method but, in the meantime, we shall review the subject in the light of Wells's comments.

Yours, etc.,
A. R. Constable,

Department of Medical Physics,
St. Paul's Hospital,
London WC2

R. W. Cranage.

Medical Physics Department,
Musgrove Park Hospital,
Taunton.
(*Received May 1981*)

Use of diagnostic ultrasound to measure the lumbar spinal canal

The Editor—Sir,

Since Porter (1978) published his experience of ultrasound examination of the lumbar spinal canal by the use of a dorsal approach, there has been great interest among orthopaedic surgeons in this possibility of obtaining an objective measure of the spinal canal. Several letters to the Editor of this Journal reflect this. Our opinion, however, is that this debate has lost its structure. A discussion about accuracy and reproducibility of the measurements has been combined with a discussion about the clinical value of the measuring method and a discussion about which structures are depicted. We think it would be advantageous to separate these discussions.

In his first paper, Porter claims that he is studying skeletal structures—the laminae. In their experimental work, Stockdale and Finlay (1980) seem to use the same presumption. Our own conclusion, after studying autopsy specimens, is that the signals which are obtained arise at the interface between cerebrospinal fluid and surrounding soft tissue structures. We believe that when this question has been settled, the question about accuracy and reproducibility will also be solved.

The value of the ultrasound method in clinical work has been mentioned by Porter as the benefit of having data available in order to make decisions about therapy of lumbar back disorders, based on clinical findings. We think that a support of that kind might be valuable in certain situations. The data so far obtained, however, cannot be used as a basis for decisions about diagnosis as far as is known today. Our experience, when evaluating spinal stenosis with the aid of ultrasound compared with myelography, is fairly disappointing (Kadziolka *et al.*, 1981).

Ultrasound examination of the spinal canal is nevertheless an important addition to the methods available for the study of the lumbar spine, as demonstrated by Porter's population study. Continuous studies of random samples of different patient populations combined with prospective evaluation of clinical data may well add important knowledge on the epidemiology of different lumbar back disorders. We are convinced that it would be within this area that ultrasound examination of the back will show its greatest value.

Yours, etc.,
A. Nachemson,
M. Asztély.

Departments of Orthopaedic Surgery
and Diagnostic Radiology,
University of Göteborg,
Sahlgrenska sjukhuset,
S-413 45 Göteborg,
Sweden.
(*Received July, 1981*)

REFERENCES

Kadziolka, R., Asztély, M., Hanai, K., Hansson, T. and Nachemson, A., 1981. Ultrasonic measurement of the lumbar spinal canal—the origin and precision of the recorded echoes. *Journal of Bone and Joint Surgery* (in press).

Porter, R. W., Wicks, M. and Ottewell, D., 1978. Measurement of the spinal canal by diagnostic ultrasound. *Journal of Bone and Joint Surgery*, *60B*, 481–484.

Stockdale, H. R. and Finlay, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101–1102.

(*Author's reply*)

The Editor—Sir,

Professor Nachemson rightly suggests that there are several areas worthy of discussion when considering ultrasound measurement of the spinal canal. Accuracy and repeatability relate to the degree of confidence that a clinician can place upon the canal measurement.

Our mean repeatability is less than half a millimetre, but the parameter measured for one patient may not be the same as for another, and any particular measurement may therefore have a one or even two millimetre error. The clinical

Correspondence

application for an individual patient investigation is likely therefore to be of less value than its help in understanding the pathogenesis of some back pain syndromes from large population studies.

It does not, however, exclude its use in individual patient management. In practice, all our back pain patients are measured, with greatest interest in those who are at the extreme ends of the range. It complements other investigations, often makes sense of the history and examination, but should not be over-valued.

The Swedish suggestion that the echoes arise from the dural interface is not supported by our experimental and theoretical work, but is an interesting concept and certainly requires clarification.

Yours, etc.,
R. W. PORTER.

Doncaster Royal Infirmary,
Doncaster DN2 5LT.

(*Received August 1981*)

Radiation dose from human platelets labelled with indium-111

THE EDITOR—SIR,

In response to comments by Mr. T. Smith (MRC Clinical Research Centre, Harrow, Middlesex) on our paper (van Reenen *et al.*, 1980), we would like to report as follows.

With regard to the cumulated blood activity, we did not use the total cumulated activity of 95.1 MBq h. The cumulated activity listed in Table I was obtained by accepting a linear removal of activity from the blood as published by Heyns *et al.* (1980).

The data used for the individual subjects were calculated by a computer program, using raw data as input. However, we overlooked the fact that because all blood samples were counted on the same day, an automatic decay correction was done. The data were therefore accepted as uncorrected, and explain the higher cumulative activity used to obtain the values listed in Table II. The blood's dose contributions to the various organs are therefore higher than the actual contribution.

We therefore admit that our data in Table II listing the dose contributions of the blood to the target organs are overestimates. We have recalculated these values and they are listed in Tables A and B. It is fortunate that the dose reported in our publication is higher than the actual, but this does not change the conclusions made using these values.

With regard to a second point, that our $\Sigma W_T \neq 1$, it is not very clear how one should handle this situation. We have initially calculated the dose to the rest of the body, but since this value was low compared to the other organs, we decided to ignore it.

For convenience, we have recalculated the dose equivalent including and excluding the whole body dose. The results are 0.54 and 0.62 mSv/MBq respectively. Taking all approximations made for dose calculations into consideration, our conclusion is that 8.6 MBq (230μCi) is within the accepted dose limit.

Yours, etc.
O. R. VAN REENEN.

Department of Biophysics,
University of the Orange Free State,
Bloemfontein, South Africa.
(Present address: Medical Physics Department, University of Medunsa, Transvaal, South Africa.)

(*Received November 1980*)

REFERENCES

HEYNS, A., DU P., LOTTER, M. G., BADENHORST, P. N., VAN REENEN, O. R., PIETERS, H., MINNAAR, P. C. and RETIEF, F. P., 1980. Kinetics, distribution and sites of destruction

TABLE A

AVERAGE RADIATION DOSE CONTRIBUTIONS (mGy/MBq) OF THE INDIVIDUAL SOURCE ORGANS TO THE TARGET ORGANS

	Source organs			
Target organs	Spleen	Liver	Blood	Total dose (mGy/MBq)
Spleen	7.163 ±2.529	0.017 ±0.004	0.092 ±0.015	7.271 ±2.523
Liver	0.024 ±0.008	0.765 ±0.163	0.088 ±0.014	0.876 ±0.163
Testes	0.002 ±0.000	0.001 ±0.000	0.063 ±0.015	0.066 ±0.015
Ovaries	0.011 ±0.002	0.009 ±p.002	0.096 ±0.015	0.116 ±0.013
Red Marrow	0.034 ±0.012	0.024 ±0.005	0.103 ±0.016	0.0162 ±0.017
Whole body	0.052 ±0.018	0.039 ±0.008	0.078 ±0.012	0.169 ±0.018
	±1SD	±1SD	±1SD	±1SD

TABLE B

DOSE RECEIVED BY THE VARIOUS TARGET ORGANS (mGy/MBq)

Subject	Sex	Spleen	Liver	Total body	Red marrow	Ovaries	Testes
AudPH	M	10.936	0.832	0.200	0.189		0.076
PNB	M	9.749	0.617	0.158	0.145		0.055
EL	F	5.398	0.990	0.177	0.178	0.133	
AF	F	6.411	0.948	0.163	0.156	0.111	
EM	F	6.609	1.073	0.163	0.151	0.103	
MM	F	4.521	0.797	0.151	0.154	0.117	
Average		7.271	0.876	0.169	0.162	0.116	0.066
±1SD		±2.523	±0.163	±0.018	±0.017	±0.013	±0.015

1981, *British Journal of Radiology*, *54*, 1012–1013

of indium-111-labelled human platelets. *British Journal of Haematology*, *44*, 269–280.
van Reenen, P. R., Lotter, M. G., Minnaar, P. C., Heyns, A. Du P., Badenhorst, P. N. and Pieters, H., 1980. Radiation dose from human platelets labelled with indium-111. *British Journal of Radiology*, *53*, 790–795.

Choosing between two formulations of a dose/cure function

The Editor—Sir,

Porter (1980) has recently presented an admirably detailed account of statistical methods for the analysis of dose/cure relationships, based on the single clonogen theory of tumour recurrence (Suit *et al.*, 1965). When the conditions of study are demonstrably those postulated by the single-clonogen theory, the analyses of dose/cure relationships proposed by Porter are more informative than those based on logistic regression. We think, however, that there are reasons for preferring logistic regression of tumour control data.

First, there is very little observable difference between the dose/cure function proposed by Porter and the logistic function in common use, despite the different forms of the estimating equations. Both are S-shaped curves adjusted so as to fit a collection of data points as closely as possible. Take for example the hypothetical data sets which Porter (1980) has generated on the assumption that the single-clonogen postulates hold. His J is a TCD(36.8). We have used those data to compute the TCD(36.8) using a logistic regression of cure probability on the logarithm of dose and compared that estimate to J as estimated by Porter, with the following results.

Source of data (Porter, 1980)	J, krad (Porter)	TCD(36.8) krad (logistic regression)
Table 1.3	4.889	4.983
1.4	4.890	4.904
2.4(2)	2.325	2.316

Because of the way in which Porter generated his hypothetical data, his procedure provides the best possible estimates of J for those data. Nonetheless, as shown above, logistic regression provides estimates of J which differ from Porter's by less than 2%. This conclusion extends to points on the dose/cure curve other than the TCD(36.8). Figure 1 reproduces Porter's dose/cure curve, and also shows a logistic dose/cure curve fitted to Porter's data (his Table 1.3). The concordance is close.

Second, in experimental tumour systems, we do not know that the single-clonogen model reflects biological reality. Indeed, where the tumour is immunogenic, the radiation dose corresponding to, say, the TCD50 would be expected to have substantial numbers of cells surviving (Suit and Order, 1974). Accordingly there is little *a priori* reason to prefer an analysis based explicitly on the model's assumptions, particularly when such an analysis does not result in marked improvement in the description of observed phenomena.

Third, as a consequence of the close similarity of the predicted results under the two analytical procedures, it is most unlikely that tumour-control experiments could be performed which would permit a clear basis for deciding which method was superior. Other considerations must apply, such as those of study design and flexibility of analysis. His parameterization of the dose/cure curve leads Porter to propose asymmetric study designs. In particular he suggests that an optimum two-group design would place 36% of animals at a dose with a cure probability of 0.028 and 64% of animals at a dose with a cure probability of 0.883. Porter's analysis (like logistic regression) yields no estimate of J in a two-group design if either group has 0% or 100% cure rate. If an investigator were to undertake a dose level study with 100 animals (a fairly large and expensive study), using Porter's "optimum" dose-level design, his chance of finding no cure in the low-dose group (and thus no estimate of J) would be $(1-0.028)^{36}=0.36$. That is, an "optimally" designed study with what appears to be a large group of animals yields no result 36% of the time. This design certainly can be improved upon either by allocating experimental animals to less extreme doses than those suggested by Porter or by distributing animals over a larger number of dose points spaced between those suggested by Porter. Indeed Porter proposes other designs in his "Advice to experimenters."

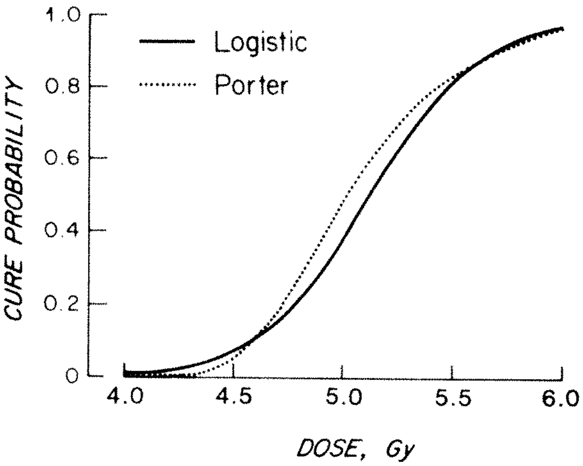


Fig. 1.

Dose/cure functions obtained for Porter's data (Porter, 1980, Table 1.3) estimated by logistic regression (solid line) and by Porter's procedure (broken line).

A final reason for preferring logistic regression is a practical one. Since logistic regression has found wide application in other fields, there are at present many commercial computer programs available which permit the investigator a flexibility of analytical approaches which have been relatively little explored in radiation biology. An important example of these is multiple logistic regression (Walker and Duncan, 1967), whereby animal and experimental characteristics other than radiation dose can be examined as independent or interactive predictors of cure rate.

Since logistic regression and Porter's proposed analyses yield essentially identical results, since study designs based on a serious acceptance of Porter's calculations can be very inefficient, and since very flexible logistic regression techniques are now available, we think that investigators should consider retaining logistic regression procedures for the analysis of dose/cure functions.

Yours, etc.,

A. M. Walker,
H. D. Suit.

Division of Biostatistics and Epidemiology,
Sidney Farber Cancer Institute,
Harvard School of Public Health,
Boston, MA 02115, USA,
Department of Radiation Medicine,
Massachusetts General Hospital,
Boston MA 02114, USA

(*Supported by Grants CA 13311 and CA 06516 from the National Cancer Institute, DHEW*)
(*Received July 1981*)

REFERENCES

PORTER, E. H., 1980. The statistics of dose/cure relationships for irradiated tumours. *British Journal of Radiology, 53,* 210–217, 336–345.

SUIT, H. D. and ORDER, S., 1974. Considerations in the interactions of radiation on immunotherapy. In *Interaction of Radiation and Host Immune Defense Mechanisms in Malignancy* (Conference, March 1974, Greenbrier, W.VA.), BNL 50418 (Brookhaven National Laboratory Report).

SUIT, H. D., SHALEK, R. J. and WETTE, R., 1965. Radiation response of C3H mammary carcinoma. In *Cellular Radiation Biology,* (Williams and Wilkins, Baltimore), pp. 514–530.

WALKER, S. H., and DUNCAN, D. B., 1967. Estimation of the probability of an event as a function of several independent variables. *Biometrika, 54,* 167–179.

(*Author's reply*)

THE EDITOR—SIR,

Walker and Suit are quite right in their first point. Logistic analyses do give reasonable approximations. But here the logistic curve is incoherent with the biological interpretation, and incoherent methods should not be used if coherent methods are available. For one thing you are deprived of the chance of finding out if your method really is coherent: a biological question.

Immunogenic tumours are indeed a whole different can of worms. I believe them to be irrelevant to human cancer, and if this is right neither Dr. Suit nor myself need waste time on them. Still, they certainly can behave in ways that subvert the logistic curve as badly as Mather's curve. I entirely agree with the third point made by Walker and Suit, which in effect proves that my discussion of experimental design was sadly obscure. My object was to illustrate the kind of influence that statistical methods should have on experimental design; practical advice came in a different section. I apologise for provoking this misunderstanding.

The final reason given by Walker and Suit for preferring logistic analysis simply staggers the mind. There are no words to express the plight of a statistician who will not write his own computer programs, but is confined to the hack-work of using commercial packages. I thought the breed was extinct.

Yours, etc.,
E. H. PORTER.

Belvidere Hospital,
Glasgow G31 4PG.

(*Received July 1981*)

Book review

Lecture Notes in Biomathematics. Questions of uniqueness and resolution in reconstruction from projections. By Myron B. Katz, pp. ix + 175, 1978 (Springer-Verlag, Berlin/Heidelberg/New York), DM 21.50, $11.80.
ISBN 3-540-09087-8

These notes provide a readable account of a mathematical exploration into the uniqueness of reconstructions obtained from projection data. It is shown how a particular set of projection angles is the least demanding on the resolution of the data, and that providing this set is used the limitation on the resolution of the reconstruction, which is necessitated by the requirement for a unique solution, may be demonstrated. It is shown how to deal effectively with noisy data and to choose the optimum projection angles under practical working conditions. A chapter on improving the EMI head scanner provides a practical application of the theory.

The work is clearly presented with adequate illustrative material and the proofs of propositions are not allowed to disturb the logical development of an idea. Much background material on practical aspects of medical image reconstruction is summarized in an appendix.

The book is intended for researchers in the general field of image reconstruction and also interested physicians. However, the treatment requires additional mathematical knowledge and expertise, and it is unlikely that many of the latter will be able to cope. This is a useful small volume for the shelf of the CT technical specialist.

M. F. COTTRALL.

Erratum

A catheter system for the safe and efficient delivery of tissue glues (bucrylate) for visceral embolization (M. S. Khangure, H. T. ApSimon, T. M. H. Chakera and D. E. Hartley), *The British Journal of Radiology,* August 1981, *54,* 671–673.

We regret that the caption to Figure 3 (p. 672) is incorrect. It should read:

Assembled catheter arrangement. (1) The balloon and tip of balloon catheter unit introduced coaxially through the guiding catheter. (2) The guiding catheter. (3) Teflon introducer sheath. (4) Y connector attached to introducer sheath. The straight limb allows the introduction of the guiding catheter. The side arm is used to flush the sheath intermittently with heparinized saline. (5) Y connector attached to the end of the guiding catheter. The straight limb is used for the introduction of the balloon catheter unit. (6) The side arm is used for the intermittent perfusion of heparinized saline into the guiding catheter. (7) 1 ml syringe containing contrast medium for balloon catheter. (8) 1 ml syringe containing opacified bucrylate. (9) Two way tap used to keep balloon inflated.

1981, *British Journal of Radiology*, *54*, 1014–1024

Proceedings of The British Institute of Radiology

Thirty-ninth Annual Congress, April 9–10, 1981

Abstracts of papers presented at The British Institute of Radiology Annual Congress held at The Royal Free Hospital School of Medicine, London NW3

Methods of monitoring response to tumour treatment

Chairman: Dr. J. Hinton

The quantification of therapeutic response in experimental tumours, by G. G. Steel.
Conventional radiology, by J. S. Macdonald.
Monitoring therapeutic response by computed tomography, by Janet Husband.
Assessment of tumour response using isotopes and ultrasound, by D. O. Cosgrove.
The clinical significance of measurement of tumour response, by Ann Barrett.

THE QUANTIFICATION OF THERAPEUTIC RESPONSE IN EXPERIMENTAL TUMOURS

By G. G. Steel

Institute of Cancer Research, Sutton, Surrey

The predicament in cancer research is that although experimental treatment and measurement of tumours in animals is much easier than in man, the systematic differences between tumours in man and laboratory animals present serious problems in translation of results between the species. It is a widespread hope that detailed studies in mouse tumour systems combined with the limited data on human tumours will lead to useful advances. To some extent the use of human tumour xenografts in immune-suppressed mice may help in this process. The methods of monitoring response in rat and mouse tumours fall into two main categories: *in situ* measurement of tumour growth-delay or cure, and the measurement of surviving fraction of clonogenic cells after tumour excision. Each of these has its own particular advantages and disadvantages; and the best approach is probably to use both types of measurement in an attempt to seek common conclusions.

From the studies that have already been made using growth delay and clonogenic cell survival in human tumour xenografts it is already clear that these tumours retain some of the characteristic properties of their source tumours in man. They provide tumour systems whose level of drug response is comparable with that found in man.

The picture that is emerging of the response of experimental tumours (including xenografts) to chemotherapy is of a wide range of cellular sensitivities to drugs, with some evidence that individual patients who clinically have the same disease may differ in their response to particular drugs.

CONVENTIONAL RADIOLOGY

By J. S. Macdonald

Royal Marsden Hospital, Sutton, Surrey

Conventional radiology is the most widely used method of assessing tumour response and behaviour in patients. Radiology enables the study of the tumour in its natural environment which is man. The behaviour of some tumours under free growth conditions and following treatment can be watched and, in selected cases, measured quite accurately. This gives information about their doubling times (Collins *et al.*, 1956; Breur, 1966; Macdonald *et al.*, 1966; 1968; Shackney *et al.*, 1978) which would seem to be the same for any individual tumour when it is free to grow in lung, soft tissue and lymph nodes. These findings help in the appreciation of the natural history of tumours; where the doubling times show reasonable clustering they allow risk periods to be defined. Growth delay can be important when assessing new forms of treatment (Ash *et al.*, 1979).

Cure can only be assumed if the tumour and deposits disappear from sight and do not return within the known risk period for that particular tumour. The resolving power of radiology is, however, poor; although under the best conditions a deposit can be followed on treatment down to a defect in an opacified node of 1 mm in diameter, this can still contain 10^6 tumour cells (Collins *et al.*, 1956). Clinical evaluation can never have the precision of laboratory experiments, but truth should not be shunned because absolute truth is not attainable and the extensive use of conventional radiology is justified because it contributes to our knowledge of the natural history of tumours and their deposits, it helps monitor the failures and successes of treatment regimes and it helps to give relatively early warning of recurrence.

REFERENCES

Ash, D. V., Peckham, M. J. and Steel, G. G., 1979. The quantitative response of human tumours to radiation and misonidasole, *British Journal of Cancer*, *40*, 883–889.

Breur, K., 1966. Radiosensitivity of human tumours II. *European Journal of Cancer*, *2*, 173–188.

Collins, V. P., Loeffler, R. F. and Tivey, H., 1956. Observation on growth rates of human tumours. *American Journal of Roentgenology*, *76*, 988.

Macdonald, J. S., 1966. In *Radiological Methods of Measurement in Clinical Evaluation of Breast Cancer*. Ed. by Hayward and Bullbrook (Academic Press, London), pp. 11–32.

Macdonald, J. S., Langier, A. and Schlienger, M., 1968. Observations on the growth of tumours in lymph nodes changing from normal to abnormal while remaining opacified after lymphography. *Clinical Radiology*, *19*, 120–127.

Shackney, S. E., McCormack, G. W. and Cuchural, G. J., 1978. Growth rate patterns of solid tumours and their relation to responsiveness to therapy. *Annals of Internal Medicine*, *89*, 107–121.

Proceedings of The British Institute of Radiology

MONITORING THERAPEUTIC RESPONSE BY COMPUTED TOMOGRAPHY

By Janet Husband

Royal Marsden Hospital, Sutton, Surrey

There is considerable overlap of the information provided by conventional radiology and ultrasound with that obtained from computed tomography, and in centres where all these techniques are available it is important to define those clinical situations where CT is the method of choice for monitoring response to treatment. Clearly, CT is ideally suited for follow-up of patients with both primary and secondary brain tumours and paranasal sinus tumours where clear demarcation of tumour boundaries and bone destruction can be shown. Although the plain chest radiographs and linear tomography provide adequate information regarding regression and growth of pulmonary metastases and mediastinal tumours in the majority of patients, CT is essential for the assessment of occult mediastinal and lung lesions. Thus, for example, in patients with obvious multiple pulmonary metastases the plain chest film is used for follow-up purposes in the initial stages of treatment, but when the chest film has returned to normal CT should be carried out to determine, as far as possible, whether the patient is in complete remission or not.

In the abdomen and pelvis both ultrasound and CT can be used to assess changes in size and structure of soft tissue tumours which are not accessible to conventional radiology, but not infrequently a tumour is demonstrated better by one technique than another. Thus, in patients with bone tumours such as Ewing's sarcoma, CT demonstrates the precise extent of the surrounding soft tissue mass as well as the degree of bone destruction, sclerosis and final remodelling. All this information cannot be provided by any other single technique.

Apart from qualitative assessment of therapeutic response, CT can be used to obtain quantitative information regarding changes in tumour volume and mean CT numbers (Husband *et al.*, 1981). Measurements of tumour volume are made using the EMIPLAN 7000 outlining the area of the tumour with a touch-sensitive light pen directly on to the CT image. The process is repeated on sequential slices throughout the tumour length and a computer programme calculates the total tumour volume. Errors of this method include the algorithm used, the pixel size and the observer's ability to obtain reproducible results *in vivo*; the major limitations are the difficulty in defining precise tumour margins and separating normal structures of similar density from the tumour mass. We have estimated tumour volume regression of abdominal nodal masses in a group of 20 patients with testicular teratomas and have also documented changes in the mean CT number of the tumour. These initial results show that reduction in tumour size is accompanied by a significant reduction in the mean CT number in the majority of patients (from solid to cystic range) but occasionally tumours which undergo cystic change during treatment increase in size. In these patients subsequent surgical excision of the mass has shown no evidence of malignancy, indicating that an increase in tumour size does not necessarily indicate progressive disease. Thus, from the preliminary results it is clear that account should be taken of the changes in internal structure of the tumour as well as changes in tumour size when assessment of response to treatment is being made. Further studies are required to determine whether these findings are characteristic of testicular teratomas or whether CT can provide useful information regarding changes in tumour structure as well as changes in volume in other tumour types.

REFERENCE

HUSBAND, J., HOBDAY, P. and CASSELL, K. J., 1981. Quantitation of therapeutic response. In *Computerized Axial Tomography in Oncology*. Ed. by J. E. Husband and P. A. Hobday (Churchill Livingstone, Edinburgh), pp. 176–186.

ASSESSMENT OF TUMOUR RESPONSE USING ISOTOPES AND ULTRASOUND

By D. O. Cosgrove

Royal Marsden Hospital, Sutton, Surrey

Of the currently assessable changes in tumours as they respond to treatment, changes in volume and structure are the province of the anatomical imaging techniques, while measures of tumour function are potentially amenable to isotope techniques. A development in the near future may allow the chemical composition of the tumour to be assessed using nuclear magnetic resonance.

Isotope studies characteristically indicate tissue handling of tagged pharmaceuticals; any anatomical information is a more or less useful by-product only. Ideally, agents that monitor specific tumour function are required, preferably showing greater affinity for more malignant tumours so that an index of tumour aggressiveness is built in. Available agents fall short of this goal but the development of anti-tumour antibodies and perhaps of nucleic acid markers may bring us a step closer. The best agent currently available is the classic radioiodine used in the well-differentiated thyroid tumours. It is part of the routine for diagnosis and management of metastatic tumour as well as being used in internal radiotherapy. Gallium (^{67}Ga) has a still poorly-understood affinity for tumours that can be useful in some situations. It will allow the detection of tumour within a fibrous tissue mass and forms a useful adjunct to a chest radiograph for treated bronchial carcinomas where it will allow recurrence to be detected early. More often the best radiopharmaceuticals available only indicate a host tissue response rather than the tumour itself. Bone and brain scans are examples. From this it is often possible to form an impression of how the tumour is behaving but this is a second-best estimate. The major limitation to the application of isotopes in this area is the availability of useful pharmaceuticals, but the imaging equipment has limited resolution and, more importantly, limited ability to quantitate isotope distribution. The introduction of emission computer-assisted tomography improves both of these weaknesses.

Ultrasound, like the other anatomical imaging systems, can be used to measure tumour volumes with a high degree of accuracy. Its use is limited chiefly to superficial and abdominal masses because structures that are covered by gas and bone are inaccessible to ultrasound. In many respects it is complementary to conventional radiology and CT, though it does have a special ability to provide information on the detailed internal texture of masses and other tissues. Usually when a tumour responds to treatment it simply shrinks, but occasionally its "echo-texture" alters with the development of fluid-like portions or of strongly reflective portions. Cystic change and fibrosis or fatty infiltration seem likely explanations for these observations. On the dual supposition that computer analysis of the ultrasound images may reveal changes in texture too subtle for the eye to detect and that such changes might have prognostic significance, research programmes into tissue characterization have been initiated with interesting initial results. Analysis of other components of the reflected ultrasound than simply the echo amplitude are also being undertaken with promising results. An additional ultrasonic technique that may have a special role in tumour assessment is Doppler used to assess tumour vascularization.

THE CLINICAL SIGNIFICANCE OF MEASUREMENT OF TUMOUR RESPONSE

By Ann Barrett

Royal Marsden Hospital and Institute of Cancer Research, Sutton, Surrey

Measurements of tumour volume may be used to determine response to treatment and to decide how long it should continue. Early response is considered by some authors to predict long term control and high-risk patients may be selected for more intensive treatment. Measurement of regression rates and growth delay may enable the clinician to compare the effectiveness of new treatments. For adequate assessment the tumour mass must have well defined margins.

As tumour volume is measured during treatment, differing responses may be seen. Reduction in size may indicate response and serial investigations will indicate how long treatment must be continued. Careful monitoring will then show whether complete tumour eradication has been achieved or growth delay only obtained.

If regression ceases or regrowth occurs, treatment can be modified as appropriate. Increasing fibrosis may lead to reduction in tumour volume but this is usually a late effect. Necrosis within a tumour or remodelling of bone may also produce apparent changes in size. Spontaneous fluctuations in tumour volume, as for example in some non-Hodgkin's lymphomas, may lead to the false impression of response to treatment.

If no change in tumour volume is seen this may reflect failure of treatment, slow regression (for example, carcinoma of the prostate) or cell killing in the tumour balanced by regrowth during therapy. In very fibrotic tumours cell killing may produce little change in apparent tumour volume. Increase in tumour volume may indicate progression of disease or haemorrhagic or cystic degeneration in the tumour. CT scanning is invaluable in monitoring tumour volume but reduction in volume does not necessarily indicate cure of the disease. The rate of tumour regression appears to predict long term control in head and neck and cervical carcinoma but not for pancreatic or bronchial lesions.

Quantitative endpoints are needed to compare new treatment regimes. Patients with multiple measurable metastases can be used in such studied and response assessed by measurement of regression rates and growth delay.

More accurate definition of tumour volume has improved radiotherapy treatment planning. Tumour marker measurements (if appropriate) are the most sensitive way of detecting tumour. The amount of marker and the rate of fall with treatment may predict response. Marker measurements however give no information as to site of disease.

Increasingly sensitive radiological and biochemical measurements are useful only in so far as effective therapy is available; complete tumour control can only be achieved when more accurate diagnosis is matched by better treatment.

Neonatal radiology update

Chairman: Dr. J. G. B. Russell

X rays and the lungs, by J. G. B. Russell.
X rays and the trunk, by J. F. Ratcliffe and K. Levick.
Real time ultrasound of the brain, by Maureen Gowland.
Real time ultrasound of the heart, by M. L. Rigby (*no abstract received*).
Ultrasound of the trunk, by C. Metreweli (*no abstract received*).

X RAYS AND THE LUNGS

By J. G. B. Russell

St. Mary's Hospital, Manchester

Very immature babies are likely to suffer from respiratory disease. In surfactant deficiency the lungs are of small volume: this is particularly true on expiration: films deliberately exposed in full expiration may be employed to confirm a diagnosis of respiratory distress syndrome, which may be of value when it is suspected that another abnormality such as a congenital heart defect is contributing to the respiratory distress. Films of the neonate with respiratory distress are taken to look for complications, not to follow changes in severity.

The radiation dose of a neonatal chest film is minute. "Interstitial gas" in the lungs of a neonate was shown to be gas in the lymphatic channels.

The distinction between broncho-pulmonary dysplasia and Wilson-Mikity syndrome is slight and is probably non-existent. The immature lung syndrome is very uncommon. Only three possible cases were found in 70 babies born at 1000 g or less.

X RAYS AND THE TRUNK

By J. F. Ratcliffe and K. Levick

Booth Hall Children's Hospital, Manchester and Children's Hospital, Sheffield

Advances in neonatology have resulted in increased salvage of dysmature neonates.

Gas is a good contrast medium for the neonatal gastrointestinal tract, although its amount and distribution varies in different conditions. Necrotizing enterocolitis (n.e.c.) is becoming more commonplace. Radiology confirms the diagnosis and may detect its most urgent complication—perforation. A later complication is stricture formation in up to 25% of cases, which may be multiple (Virjee *et al.*, 1979). Radiographs reduce the risk of n.e.c. if the tip of an umbilical vein catheter is shown proximal to the ductus venosus.

Voluntary muscle paralysis, to reduce the risk of pneumothorax in babies on ventilators, results in no air being swallowed. The gasless abdomen in these circumstances is not a cause for alarm, providing that if gasless abdominal distension supervenes, the possibility is recognized of obstruction or perforation.

Fluid levels in meconium ileus may indicate a complication such as volvulus or n.e.c., because obstruction without fluid levels is the usual pattern in this disease.

The lower limit of gas in the rectum may not be a reliable indication of the level of rectal atresia.

The low osmolality water soluble media, such as Hexabrix or Amipaque, should always be considered for positive contrast of the neonatal gastro-intestinal tract or in peritoneography. However, in the treatment of meconium ileus Gastrografin is still the most effective agent.

Histology is now often used for the diagnosis of, and indication of the extent of, Hirschsprung's disease. Radiologists may be the first to recognize total aganglionosis of the large bowel and terminal ileum which may present atypically.

Reversible, short-lived smooth muscle relaxation may be achieved with Glucagon approximately 1 μg/kg IV (Ratcliffe, 1980). This relieves spasm for diagnostic purposes and assists double contrast examination, and may be useful in reduction of intussusception.

The use of abdominal CT scanning in neonates is extremely limited.

REFERENCES

RATCLIFFE, J., 1980. Glucagon in barium examinations in infants and children: special reference to dosage. *British Journal of Radiology*, *53*, 860–862.

VIRJEE, J. P., GILL, G. J., DESA, D., SOMERS, S. and STEVENSON, G. W., 1979. Strictures and other late complications of neonatal necrotising enterocolitis. *Clinical Radiology*, *30*, 25–31.

REAL TIME ULTRASOUND OF THE BRAIN

By Maureen Gowland

Department of Diagnostic Radiology, University of Manchester

With the introduction of aggressive neonatal intensive care in the last decade, there has been a marked increase in the survival rate of low birth-weight premature infants. These infants born before 32 weeks gestation with a birth weight less than 1500 g are particularly susceptible to sub-ependymal and intraventricular haemorrhage. The clinical features of these conditions are not specific and so it is difficult to make a confident diagnosis on the clinical findings alone. Ultrasound provides an accurate method of demonstrating the presence or absence of these lesions, indicating the extent of the lesion and monitoring its course.

Using a commercially available portable linear array real-time ultrasound system with a 5 MHz probe, infants are examined in the neonatal intensive care unit. The examination is conducted without removing the infant from his incubator and with no interruption of support or monitoring systems.

The transducer array is placed vertically on the anterior fontanelle in the coronal plane. By angling the probe anteriorly and then posteriorly, both lateral ventricles and periventricular regions are outlined. The probe is turned through 90° and sagittal and parasagittal images of both lateral ventricles are obtained. In the normal brain the lateral ventricles are seen as small slit-like echo free areas on each side of the mid-line, and below the ventricles well defined areas of low echo density, the thalami and basal ganglia are clearly delineated. Sub-ependymal and intraventricular haemorrhages are well seen using this technique. The haemorrhages are graded according to their severity; grade 1 is diagnosed when an irregular group of increased echoes is demonstrated in the region of the caudate nucleus; when these echoes extend into the lateral ventricle without any associated increase in size of the ventricle, grade 2 haemorrhage is diagnosed; ventricular enlargement occurring in association with these features constitutes grade 3 haemorrhage and extension of the haemorrhage into the adjacent cortex and white matter is seen in grade 4. The situation is not static. The findings may be normal at the first examination and evidence of haemorrhage of increasing degrees of severity may be found at subsequent examinations.

At present, the significance and long term prognosis of these lesions is not fully understood, but with this, an accurate method of documenting the presence and extent of these lesions, long term follow-up of infants who survive these lesions will complete the picture and the full implication of sub-ependymal and intraventricular haemorrhage in the premature infant will be appreciated.

Validation of nuclear cardiology

Chairman: Dr. K. E. Britton

Equilibrium gated studies: validation of parametric scanning, by N. W. Garvie, F. Bitter and W. E. Adams.
Clinical experience with phase analysed gated cardiac studies, by S. Walton and P. J. Ell.
Validation of stress testing in nuclear cardiology, by R. J. Wainwright, D. A. Brennand-Roper and M. N. Maisey.
Clinical experience with stress testing in equilibrium gated cardiac studies, by A. L. Muir.
Validation of first pass cardiac studies, by A. T. Elliott, D. L. Stone, D. J. Dymond and A. Abdullah (*no abstract received*).
Myocardial perfusion and metabolism: quantitation in patients using positron tomography, by A. P. Selwyn.

EQUILIBRIUM GATED STUDIES: VALIDATION OF PARAMETRIC SCANNING

By N. W. Garvie, F. Bitter and W. E. Adams

Nuclear Medicine Department, University of Ulm, Germany

With gated blood pool techniques (GBP) various techniques of analysis may be employed. In the present study the time activity curve of each individual pixel point was analysed in order to display the regional distribution of various cardiac parameters within the heart region. This method of analysis—known as parametric scanning—can be used to detect regional wall motion abnormalities (RWMA) of different kinds.

The "peak filling rate" scans showed the greatest sensitivity for detecting RWMA when compared with contrast ventriculography (97%) but a combination of various parametric scans (phase and amplitudes of the first Fourier coefficient of the pixel curves, end-diastolic minus end-systolic count differences, count differences between the end of the fast filling period and end systole) yielded an optimal combination of sensitivity and specificity (91%, 90%). Phase analysis proved particularly sensitive in the presence of paradoxical motion.

CLINICAL EXPERIENCE WITH PHASE ANALYSED GATED CARDIAC STUDIES

By S. Walton and P. J. Ell

Departments of Cardiology and Nuclear Medicine,
Middlesex Hospital and Medical School, London

Phase analysis of radionuclide angiocardiograms can be used to detect ventricular regions with abnormal emptying patterns. We have compared phase evaluation with cardiac catheterization data.

Eighty-six subjects underwent equilibrium radionuclide studies in the LAO projection. Twenty-six were normal and of 60 with coronary disease, 38 had total occlusion of at least one major coronary artery. Fifty-one subjects underwent first pass radionuclide studies in the RAO projection: 18 were normal and 23 of 33 with coronary disease had total occlusion of at least one major coronary artery. Phase analysis was performed on a regional basis for all subjects.

In both equilibrium and first pass studies there was an inverse relationship between the maximum value of regional phase and the left ventricular ejection fraction. High phase values were specific for total occlusion of a major coronary artery. In the first pass study a direct comparison of regional phase values and the amplitude of regional wall motion revealed progressively higher phase values with increasing severity of wall motion abnormality. In the equilibrium study, where such comparison was not possible because of the different projection, high phase values were only found in ventricles with severe wall motion abnormalities. Both approaches were particularly suited to the detection of ventricular aneurysm and could greatly facilitate estimation of the contractile segment ejection fraction.

Phase analysis represents an important advance in the non-invasive evaluation of regional ventricular contraction patterns.

VALIDATION OF STRESS TESTING IN NUCLEAR CARDIOLOGY

By R. J. Wainwright, D. A. Brennand-Roper and M. N. Maisey

Departments of Cardiology and Nuclear Medicine,
Guy's Hospital, London SE1 9RT

Exercise ^{201}Tl myocardial scintigraphy (^{201}Tl EMS) and rest/exercise comparisons of ventricular function using ^{99}Tc^{m} multiple gated blood pool imaging (^{99}Tc^{m} GBPS) are sensitive techniques in the detection of patients with coronary artery disease. In this study of 118 patients (48 normal, 70 with coronary artery disease) ^{201}Tl EMS was compared with ^{99}Tc^{m} GBPS performed during dynamic supine exercise (DSE), isometric handgrip (IHG) and peripheral cold stimulation (CS) to determine the validity of different forms of stress. A fall of 8% in global left ventricular ejection fraction (LVEF) or impaired regional wall movement (RWM) was regarded as abnormal.

Most patients with normal coronary arteries had a significant increase in mean LVEF and preserved RWM with each intervention but false positive results occurred in 4% patients with IHG, 5% patients with CS and 20% patients with DSE. ^{201}Tl EMS was falsely positive in 8% patients.

In contrast most patients with obstructive coronary artery disease developed a significant fall in LVEF or abnormal RWM. CS was the most sensitive intervention during ^{99}Tc^{m} GBPS identifying 87% patients with coronary artery disease compared to 62% patients with both forms of exercise. ^{201}Tl EMS was abnormal in 90% patients.

Five patients with normal coronary arteries had angiographic evidence of coronary artery spasm. Only CS:^{99}Tc^{m} GBPS became abnormal in this group, probably due to cold-induced spasm of a large coronary artery.

It is concluded that: CS in resting patients is more sensitive and more convenient than IHG and DSE during ^{99}Tc^{m} GBPS and may be particularly suitable to evaluate patients with suspected coronary artery spasm in whom exercise may be an inappropriate intervention; CS:^{99}Tc^{m} GBPS has similar predictive accuracy to ^{201}Tl SMS providing a useful economy in cost of tracer.

CLINICAL EXPERIENCE WITH STRESS TESTING IN EQUILIBRIUM GATED CARDIAC STUDIES

By A. L. Muir

Department of Medicine, Royal Infirmary, Edinburgh

Gated blood pool imaging allows assessment of ventricular performance during stress. In contrast to normal subjects in whom left ventricular fraction increases during exercise, patients with coronary artery disease show no increase or even a fall in ejection fraction (EF). Concern about chest wall movement during the acquisition of the exercise data and technical difficulty in conducting dynamic exercise has led to a search for alternative stress tests, but in our hands neither pharmacological stimulation nor the ice pressor test have proved good discriminators. We continue with supine dynamic exercise as our principal stress test and illustrate its use in stable and recent onset angina and after myocardial infarction.

1. In 47 patients with stable angina the change in ejection fraction on exercise related to the number of vessels involved and to a myocardial perfusion score derived from the extent of vessel disease and the distribution of these vessels.
2. About 20% of patients with recent onset angina have a poor prognosis but identification of this subgroup has proved difficult. In 19 patients with recent onset angina EF was measured before and during supine exercise and in nine it fell by at least 0.10. In five of these nine prognosis was poor at six months and two have proceeded to infarct.
3. Following myocardial infarction ejection fraction is usually reduced. In 100 patients recovering from their first infarct a low resting ejection fraction was predictive of the subsequent development of heart failure, ventricular arrhythmias and sudden death, but not of angina. However a fall in EF on exercise was highly predictive of those likely to develop angina.

The results suggest that changes in ventricular performance during exercise may be used to predict the extent of coronary artery disease and the subsequent prognosis.

MYOCARDIAL PERFUSION AND METABOLISM: QUANTITATION IN PATIENTS USING POSITRON TOMOGRAPHY

By A. P. Selwyn

Cardiovascular Research Unit, Hammersmith Hospital,
Du Cane Road, London W12

Patients presenting with angina pectoris suffer underlying transient disturbances of regional myocardial perfusion and metabolism. These ischaemic episodes jeopardize ventricular myocardium. One role for radionuclides is to detect and quantify these disturbances for diagnosis, management and basic research into mechanisms. Single photon emissions (^{201}Tl) and the gamma camera do not provide pure physiological measures of either flow or metabolism and the gamma camera cannot quantify events in the heart. Tomography using positron emitting isotopes is able to quantify the true concentration of tracer in the myocardium non-invasively.

Rubidium 82 (derived from a generator) has been developed for intravenous infusion and used with the positron camera. This provides a measure of the regional myocardial uptake of this potassium-like cation. The short half life (78 s) allows repeated studies. Patients with angina and coronary disease have shown that the regional defects in scans during angina appear because of an absolute reduction in tracer uptake in the affected region. The regional defects due to ischaemia persist much longer than pain and the electrocardiogram suggest.

Inhalation of CO_2 (labelled with ^{15}O) is being developed for quantitation of regional myocardial perfusion and ^{11}C acetate (intravenously) is being used to assess oxidative and anaerobic processes in each region of the myocardium.

The purpose of the above research is to characterize the disturbances of regional myocardial perfusion and metabolism in patients with angina pectoris in order to understand the causes that trigger acute regional myocardial ischaemia.

This research was supported in part by the British Heart Foundation and the Wellcome Trust.

Observer performance in diagnostic radiology

Chairman: Dr. B. S. Worthington

The eye sees, but the brain knows, by B. S. Worthington.
Visual search and recognition—complexity in simplicity, by A. G. Gale.
Approaches towards an objective assessment of image quality, by P. F. Sharp.

THE EYE SEES, BUT THE BRAIN KNOWS

By B. S. Worthington

Department of Diagnostic Radiology,
University of Nottingham

The radiological task has similarities to other visual inspection problems more commonly subsumed within the province of experimental psychology including visual search, signal detection, pattern recognition and vigilance studies. Research techniques and recommendations found useful in these situations are beginning to be applied to radiology.

Pattern recognition is central to the everyday work of a diagnostic radiologist and involves matching information in the immediate memory store with that previously acquired and retained in the long term store. The study of images generated from long term memory allows inferences to be made about the ways in which information is stored and also to determine whether information is abstracted from such images in ways similar to those employed in viewing radiographs directly.

There is evidence that our memory of a particular radiological appearance is coded and stored separately in both a visual or spatial mode and also in a verbal mode. This representational format of the information stored in long term memory is well suited to the operations performed upon it. Our memory of a particular radiological appearance probably does not resemble a photographic copy, but is rather a reconstruction derived from stored information which records the spatial relationships within the image and also reflects a number of stored propositions which contain our prior interpretation of the image.

There is evidence that our processing of information derived from direct viewing of radiographs runs in parallel with a conceptually driven analysis which derives from expectations generated from within the context of the film.

The principal factors limiting the observer's capacity to process data derived from viewing radiographs include our limited memory capacity; our selective rather than comprehensive abstraction of information; our inability to integrate a great deal of information simultaneously and the fact that our inevitable simplification of judgement tasks introduces bias into decision making.

Research in this area is directed towards answering two questions: what are the activities involved in reporting radiographs? and what does learning radiology consist of? The answers to these clearly bear on understanding the cause of reporting errors and on improving our techniques for effective radiological teaching.

VISUAL SEARCH AND RECOGNITION—COMPLEXITY IN SIMPLICITY

By A. G. Gale

Division of Radiology, University Hospital, Nottingham

Examination of visual search in radiology is useful in determining some of the underlying factors of radiological performance. Introspective reports by radiologists of how they have visually examined a radiograph do not give a reliable account of their search behaviour. In order to examine this process it is thus necessary to record the eye movements of the observer.

Using this approach it has been shown that radiological experience may serve to produce patterns of search which are qualitatively different from that of a more naive observer, although such differences merit more quantitative assessment. The real effect of such experience must be in selecting the appropriate schema for the task of recognition. Instructions or clinical information serve to set up visual expectancies prior to viewing the film itself. This can affect both the search pattern and recognition performance. It is therefore advisable to search a film both before and after reading clinical information. Similar advice pertains to viewing a current film before and after reviewing previous films of the same patient. Instructions to search a film in a prescribed manner were found to be counter-productive by interfering with the individual's own cognitive search strategies.

A more confident decision about the degree of normality or abnormality of a film is not produced by permitting unlimited viewing of the radiograph as the radiologist can still be constrained by his prior visual expectancies. Thus a gross abnormality can be exceedingly difficult and frustrating to detect. At the same time radiologists can detect abnormalities in approximately a single fixation. These two extremes illustrate the problems of "looking without recognizing" and "recognizing without looking" and serve to demonstrate that the area of the radiograph which the observer is fixating is not necessarily where he is attending.

Further work in this area will lead to the clarification of such problems and will not only help current radiological practice but will enhance the training of new registrars.

APPROACHES TOWARDS AND OBJECTIVE ASSESSMENT OF IMAGE QUALITY

By P. F. Sharp

Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen

Three methods for subjectively measuring image quality were considered; the method of constant stimuli, signal detection theory and ranking/rating.

Provided that the criterion used by an observer to reach a decision on the presence or absence of an abnormality can be defined then the method of constant stimuli is useful for measuring image quality in terms of physical parameters such as minimum detectable detail size. However, it often requires that a large number of images be viewed.

Signal detection theory avoids the need to define the observer's decision criterion by measuring his ability to discriminate between two sets of images, usually normal and abnormal, in terms of the variation of true and false positive visual responses as the observer's decision criterion is changed. However, there are problems in analysing the data when correct location of the abnormality is also necessary and in defining the population of abnormal images. With some types of images it is difficult to produce a high false positive response rate and so plotting of the ROC curve becomes inaccurate. Finally the results do not indicate what true and false positive response rate an observer actually produces in clinical practice.

Ranking techniques simply require the observer to arrange a set of images in order of quality. This avoids the need to define quality in terms of a specific task, such as the ability to detect an abnormality, but does not give a numerical measure of quality.

With rating methods quality is quantified by assigning scores to particular parameters associated with quality *e.g.* an image with good contrast would be given a higher score than one with poor contrast. The overall quality of an image is then given by the sum of these individual scores. Choice of score values poses a problem.

Good cosmetic results and cure?

Chairman: Dr. K. E. Halnan

Optimization of skin treatments, by Margaret Spittle (*no abstract received*).
Treatment of soft tissue and bone sarcomas, by Jill A. Bullimore (*no abstract received*).
Aesthetic results in breast carcinoma treated by irradiation, by J. R. Vilcoq, R. Calle and P. Schlienger.
The cosmetic and functional effects of fast neutrons in the treatment of tumours of the face, by Mary Catterall and R. D. Errington.
The place of surgery in the management of tumours of the head and neck, by E. N. Gleave.

AESTHETIC RESULTS IN BREAST CARCINOMA TREATED BY IRRADIATION

By *J. R. Vilcoq, †R. Calle and *P. Schlienger

**Radiotherapy Service "C" and †Medical Section, Institut Curie, Paris*

Since 1960, following the work carried out by Baclesse and Taillefer at the Curie Institute, we have applied radiotherapy to breast cancer operable at first (T1, T2, T3 10 cm, N0, N1a, N1b), *i.e.*, either lumpectomy plus irradiation (T1, T2 3 cm, N0, N1a) or exclusive irradiation T1, T2, N1b, T3 N0, T3 N1b). Complementary surgery is performed when complete sterilization has not been obtained immediately after the treatment or in the case of recurrence and 953 cases have survived at least five years.

Techniques of treatment and five- and ten-year-survival were described. Cosmetic results have been evaluated in 252 cases relating to patients with a ten-year survival. We divided these cases into three groups: excellent to good, good to fair, poor.

The cosmetic results have been determined in correlation with (1) the therapeutic protocol chosen, *i.e.* either lumpectomy plus irradiation or exclusive irradiation. The best cosmetic results have been obtained by lumpectomy plus irradiation (good results in 77%, whereas for exclusive irradiation only 45%); (2) the size of the breast: the smaller the breast and the smaller the field of irradiation, the better the cosmetic results obtained; (3) the dose.

Conclusion: if the breast is small or average; if the field of irradiation is small; if the protocol chosen is lumpectomy plus irradiation; if the patient is treated by ^{60}Co and the dose to the breast is lower than 6400 cGy (rad) we have good reasons to expect excellent or good results.

THE COSMETIC AND FUNCTIONAL EFFECTS OF FAST NEUTRONS IN THE TREATMENT OF TUMOURS OF THE FACE

By Mary Catterall and R. D. Errington

MRC Cyclotron Unit, Hammersmith Hospital, Du Cane Road, London W12

Fast neutrons differ significantly from photons both biologically and in their physical interaction with matter. They are two to three times more effective against hypoxic cells and, relative to muscle, they are more absorbed by fat and less absorbed by bone than are photons. The latter means that where tumours are of soft tissue and are in or near bone, an advantageous therapeutic difference exists between the normal bone and tumour when neutrons are used (Catterall and Bewley, 1979).

The importance of hypoxia as a cause of failure in local cure has been illustrated by the hyperbaric oxygen trials (Henk *et al.*, 1977) where significantly better tumour control was achieved when conventional radiotherapy was given in hyperbaric oxygen. The importance of preserving facial bones, in contrast to their removal by radical surgery for tumours of the mouth and paranasal sinuses, is seen in the avoidance of severe disfigurement and disability of talking, eating and drinking which are the sequelae of surgery. In malignant parotid-gland tumours the facial nerve is nearly always severed by surgery with very disabling results.

Fast neutrons have been used in 117 cases of stage 3 and 4 tumours of the oral cavity, oropharynx, salivary glands and paranasal sinuses. There was complete regression of tumour for more than one year in 86%, 100%, 92% and 75% of cases respectively and the overall recurrence rate was 12.5%. Serious complications arose in 16% but this figure would be reduced if less advanced and therefore smaller tumours were treated. Biopsy after neutron therapy precipitated necrosis in six cases (all negative for tumour) and so is contraindicated. These six cases are included in the 16% complication rate.

The value of the low absorption of neutrons in bone is shown by the absence of radiation induced necrosis and the remodelling of eroded bone after regression of the tumour. These factors enable dentures to be worn and speaking, eating and talking are normal. In salivary gland tumours the facial nerve has never been damaged and indeed recovery of function occurs when the tumour mass resolves, provided that paralysis has not been present for more than 2 months.

The control rate using neutrons is very high even in advanced tumours and the cosmetic and functional results are very good. There are strong indications for controlled clinical trials comparing neutrons with surgery in operable cases and neutrons with iridium implants in carcinoma of the tongue. In the meantime, fast neutrons have a major contribution to make in the treatment of tumours in the face.

REFERENCES

CATTERALL, M. and BEWLEY, D. K., 1979. *Fast Neutrons in the Treatment of Cancer* (Academic Press, London; Grune & Stratton, New York).

HENK, J. M., KUNKLER, P. B. and SMITH, C. W., 1977. radiotherapy and hyperbaric oxygen in head and neck cancer: final report of the first controlled clinical trial. *Lancet, ii*, 101–103.

THE PLACE OF SURGERY IN THE MANAGEMENT OF TUMOURS OF THE HEAD AND NECK

By E. N. Gleave

Christie Hospital and Holt Radium Institute, Manchester

Surgery is used most frequently in the management of primary tumours of the head and neck after radiation therapy has failed, when tumours are residual or recurrent, and for major necrosis following irradiation. There are special indications for primary surgery but they are uncommon. The extent of surgery must often be radical in order to obtain a margin of clearance around a tumour and removal of previously irradiated tissue so that repair can be done between normal tissues, although lesser procedures can sometimes be used. Cervical lymph nodes involved by metastatic tumour are better treated surgically by block dissection which is often incorporated as part of a resection in continuity.

There have been many advances in the technique of reconstructive surgery within the last two decades. Tissue for repair may be obtained by the use of local flaps, regional flaps with axial or random blood supply, myocutaneous flaps and free flaps from a distant site with microvascular anastomosis of feeding blood vessels. Reanimation of the paralysed face can now also be achieved in several different ways.

The success of surgery must be judged not only by its beneficial effect on control of disease or provision of good palliation but also by successful rehabilitation after surgical treatment. This can only be assessed by restoration of good function and appearance. Radiation and surgery are still the only methods of cure for malignant tumours of the head and neck and are often complementary to each other. More attention should be given to the additive effects of sequential treatment rather than independent analysis since there should be no element of competition.

Proffered paper

Chairman: Dr. A. Dixon

CT SCANNING IN THE PAROTID REGION

By S. J. Golding

Department of Radiology, Royal Marsden Hospital, Sutton, Surrey

Twenty cases of swellings of the region of the parotid gland have been examined using the EMI CT 1010 Head Scanner. The technique of the examination and the abnormal CT appearances were described.

Neoplasms were demonstrated in eight patients, two of these being due to secondary deposits in the region of the parotid. The other lesions demonstrated include cystic hygroma, branchial cyst and tuberculous lymph nodes. All tumours showed significantly higher attenuation values than normal salivary tissue and contrast media, either intravenous or intraglandular, were not found to be necessary for adequate demonstration.

In all patients the precise extent of the tumour was delineated and the technique is particularly useful in planning surgery, especially in cases of tumours of the deep lobe of the parotid.

CT appears to be an accurate method of excluding macroscopic tumour at presentation or after surgery. Four patients with normal CT appearances were submitted to surgery on symptomatic grounds and subsequent histology confirmed the presence of normal salivary tissue.

Proceedings of The British Institute of Radiology

Diagnostic pathways in common conditions

Chairman: Dr. B. K. Wignall

A lump in the chest, by C. D. R. Flower (*no abstract received*).
Recurrent urinary infection in childhood, by I. Gordon.
Mild head injuries in casualty, by G. J. de Lacey.

RECURRENT URINARY INFECTION IN CHILDHOOD

By I. Gordon

*Hospital for Sick Children, Great Ormond Street,
London WC1*

The first proven urinary tract infection (UTI) warrants investigation (Aascher, 1980). The aim is adequate visualization of the kidneys and establishing the cause of the UTI. Previously an IVU and MCU were carried out (Saxena *et al.*, 1975). An abdominal ultrasound and ^{99}Tc^{m} dimercaptosuccinic acid (DMSA) scan (Merrick *et al.*, 1980) are now the base-line examinations. An MCU is required in all males and in girls under five years of age; if normal no further imaging is required. When a second UTI occurs then an IVU together with a repeat ultrasound and ^{99}Tc^{m} DMSA should be done. If these are normal then cystoscopy is needed if further UTI occurs. If the abdominal ultrasound and/or the ^{99}Tc^{m} DMSA scan are abnormal an IVU and MCU are required regardless of the child's age or sex.

The natural history of uncomplicated vesico-ureteric reflux (VUR) is spontaneous cessation with age. Renal scars only occur under four years of age and are associated with intrarenal reflux and infection. When VUR is detected, every child requires follow-up by radioisotope cystogram, either the direct or indirect method (Conway *et al.*, 1974).

Following ureteric surgery follow-up is by ^{99}Tc^{m} DTPA scan with frusemide if necessary. When renal scarring has occurred long-term follow-up is essential because of the possibility of hypertension and/or chronic renal failure. An abdominal ultrasound coupled with ^{99}Tc^{m} DMSA scan at two yearly intervals is suggested. ^{99}Tc^{m} DTPA if combined with individual kidney GFR results needs careful evaluation.

REFERENCES

AASCHER, A. W., 1980. In *The Challenge of Urinary Tract Infections* (Grune & Stratton, New York), p. 93.

CONWAY, I. J., BELMAN, A. B. and KING, L. R., 1974. Indirect radionuclide cystography. *Seminars in Nuclear Medicine*, *4*, 197–211.

MERRICK, M. V., UTTLEY, W. S. and WILD, S. R., 1980. The detection of pyelonephritic scarring in children by radioisotope imaging. *British Journal of Radiology*, *53*, 544–556.

SAXENA, S. R., LAURENCE, B. M. and SHAW, D. G., 1975. The justification for early radiological investigations of urinary tract infection in children. *Lancet*, *ii*, 403.

MILD HEAD INJURIES IN CASUALTY

By G. de Lacey

*X-ray Department, Northwick Park Hospital and
Clinical Research Centre, Harrow, Middlesex*

A retrospective study of 130 consecutive patients referred from the accident and emergency department for skull radiography was presented.

A distinction must be made between mild and severe head injuries. The patients in this series had sustained mild injuries, and this accounts for the vast majority of the 1 000 000 patients who attend casualty each year. A distinction must also be made between head injuries in children and adults. In children there is a low association between an intracranial haematoma and a skull fracture. However, nearly 90% of adults with an intracranial haematoma have a fracture. This distinction has not always been made in the radiological literature and general observations/conclusions drawn from either the classical paediatric papers or patients of unstated age are misleading. The sensible application of clinical guidelines would undoubtedly reduce the number of X-ray films requested, but the uselessness of skull radiography has been overstated. Firstly, a depressed fracture may be impossible to detect clinically and a skull radiograph is essential if intracranial infection is to be prevented in some of these patients. Secondly, consideration should be given to the clinical use of skull films as an aid to reducing the number of adults with mild injuries admitted to hospital for observation.

Many authors have stressed the low clinical return and expense of skull X-ray films but fail to compare this with the cost of overnight admissions for observation. In 1972 there were 142 000 admissions to hospital for head injury in England and Wales and the vast majority of these were mild injuries. Moreover, admissions for head injury increased by more than 40% between 1963 and 1972, and short-stay admissions for one day or less accounted for this increase.

There remains a serious reservation that normal skull radiographs be used to help reduce admissions for observation. In this study there were four fractures in 130 patients and two were not recognized by the casualty officer. Obviously it would be unwise to suggest that casualty officers should use "normal" films to reduce admissions if a high proportion of fractures are missed. The time during which most head injuries occur has a particular importance in this regard. In children and adults they occur mainly after 5 p.m. and reach a peak at the weekend. During these times most radiologists are not in the hospital and films cannot be readily brought to them for either a second opinion or immediate reporting. At weekends it would be common for more than 24 h to elapse before a missed fracture would be reported. Nevertheless, if clinical and radiological competence in casualty were improved it should be possible to reduce both the amount of radiology as well as the number of unhelpful admissions for observation following mild head injury.

Proceedings of The British Institute of Radiology

Proffered paper

Chairman: J. F. Fowler

DIRECT MEASUREMENT OF DOSE AT DEPTH IN BREAST CANCER USING LITHIUM FLUORIDE

By P. J. D. K. Dawes, E. G. Aird, I. Crawshaw and P. Kevey

Royal Victoria Infirmary, Newcastle

A three-field technique is used to irradiate the breast and regional gland areas when the breast is to be conserved. One month later the tumour-bearing area receives a boost of radiation using ^{92}Ir as a temporary implant. It is possible before placing the iridium into the nylon tubes to use the tubes to carry LiF thermoluminescent rods. A fraction of external beam therapy is given, allowing direct measurement of the dose received at depth in the breast.

The table shows the prescribed dose, the mean measured dose and standard variation and the percentage difference between these doses in 14 cases.

The range of differences was between -15.5% and $+29\%$. If the two very wide results are excluded 12 of the 14 cases had a mean variation of 5.6% from the prescribed dose. Within some breasts there was also considerable variation about the mean. Possible explanations for the variations are first that the doses are prescribed on a central contour, second in one case no wedges were used ($+29\%$) and third treatment errors.

As this conservative technique has been developed, modifications of approximately 5% in the skin dose to reduce the acute reactions have been made. The concern must be that a similar dose variation within the breast might lead to local recurrence.

The technique described is feasible and demonstrates variations within the volume of interest. The intention is to make further modifications in the treatment technique in the light of these findings and further phantom studies and then to use LiF rods to assess the technique.

Prescribed dose (cGy)	Mean measured dose (cGy)	±1 s.d.	Difference $\frac{\text{measured}}{\text{prescribed}}$ %
202	193	20	-4.5
235	303	19	$+29$
240	265	4	$+10$
246	208	14	-15.5
247	239	6	-3.2
247	251	21	$+1.6$
248	235	5	-5.3
250	264	20	$+5.6$
250	231	14	-7.6
252	273	8	$+8$
252	250	9	-0.8
264	270	28	$+2.2$
350	314	13	-10.3
351	378	24	$+7.7$

Retreatment

Chairman: Professor R. J. Berry

Persistence of chromosomal lesions in human lymphocytes and skin fibroblasts, by J. R. K. Savage.
Ability of normal rodent tissues to tolerate retreatment, by J. V. Moore.
Retreatment by hyperthermia, by Marilyn P. Law.
Clinical aspects of retreatment, by R. D. Hunter.

PERSISTENCE OF CHROMOSOMAL LESIONS IN HUMAN LYMPHOCYTES AND SKIN FIBROBLASTS

By J. R. K. Savage

MRC Radiobiology Unit, Harwell OX11 0RD

Chromosomal aberrations can be reduced to four categories on the basis of the location of the participating lesions in relation to the chromosome arms. Those involving the interaction between two lesions may appear at metaphase in one of two forms, asymmetrical (*A*) or symmetrical (*S*).

A forms always have an acentric fragment, lead to genetic loss and sometimes mechanical problems at mitosis and are readily observed and scored with conventional staining methods.

S forms never produce acentric fragments (unless interaction of lesions is incomplete), very rarely lead to genetic imbalance, and many types cannot be observed without recourse to chromosome banding techniques.

Thus, in a dividing cell population, we expect *A* forms to be eliminated within a few cell generations, but *S* forms to persist more or less indefinitely. Both forms should persist in a non-dividing population.

These expectations are generally fulfilled. A low but significant level of *A* forms is still found in lymphocytes of atomic bomb survivors and patients who received therapy for ankylosing spondylitis 25 years ago. *S* forms remain high and steady in both groups. Several other examples can be cited, all pointing to the existence *in vivo* of some very long-lived lymphocytes.

In fibroblasts from irradiated skin, it is difficult to obtain much information about *A* forms, but an abundance of *S* forms (not all genetically balanced) has been found up to 60 years after treatment, together with a lack of evidence to suggest any selection against aberration-bearing cells for tissue repair. From work with liver, thyroid and skin, there is some indication that, given time, aberrations may be removed by repair before division. The amount of repair may differ between tissues and is quicker after X rays than after neutrons.

It is suggested that, for practical purposes, the persistent aberrations which will be present in tissues after a previous course of therapy are probably of little relevance to retreatment.

ABILITY OF NORMAL RODENT TISSUES TO TOLERATE RETREATMENT

By J. V. Moore

Paterson Laboratories, Christie Hospitql and
Holt Radium Institute, Manchester

This paper discusses data from the experimental literature pertinent to the problem of residual injury and "tolerance" to retreatment. The time scale of recovery (repair and repopulation) of normal rodent tissues after a first dose or course of radiation or chemotherapy varies widely, with repopulation intervals of days for intestinal mucosa, a few weeks for bone marrow and skin, and several weeks to months for elements in CNS, lung and bladder. In a few cases, residual injury that may affect the outcome of a second treatment given during or after the recovery phase can be demonstrated directly in terms of altered cell numbers or functional capacity. Particularly where the first treatment is given as a course (*e.g.* 1.0 to 4.5 Gy of X rays q 3 wk×4) the CFU_s of the marrow do not recover fully, either quantitatively—with the above schedule their numbers return to a plateau only 30 to 40% that of controls—or qualitatively—the average self-renewal probability of each CFU_s is only 10 to 20% of controls. This deficit persists for at least 1 year *i.e.* at least half the lifetime of a mouse. Similar effects can occur after courses of drugs, notably busulphan and BCNU. Also, in the mouse a single tolerance treatment of adriamycin reduces the capacity of cells of the intestinal epithelium to proliferate in response to subsequent irradiation, even at intervals between agents of approximately two months.

More often, evidence for residual injury has been sought in terms of altered tolerance to a second treatment measured at tissue, organ or whole-animal level: does, for example, foot or tail breakdown resulting from "connective-tissue" injury in the skin, paralysis arising from CNS injury, or thoracic lethality from lung damage, occur at the same or at lower dose levels as in non-pretreated rodents? For skin, the second dose required to elicit either "early" or "late" tolerance end-points tends to fall as a function of the increasing effectiveness of the first treatment, but to no more than 90% of the single dose producing the same degree of damage in non-pretreated animals (with the important exception of one study using 10f/11 days, where second-dose tolerance was reached at only 60%). For murine lung treated by two equal doses of X rays separated by six weeks, second dose tolerance was exceeded at 70% and for neutrons at about 60% of the single-dose equivalent. In the spinal cord two different modes of injury leading to paralysis are expressed at different times. A separation of two X-ray doses by 16 weeks yielded a second dose tolerance of 75% for white matter necrosis in the rat, but only 50% for paralysis resulting from vascular damage.

RETREATMENT BY HYPERTHERMIA

By Marilyn P. Law

MRC Cyclotron Unit, Hammersmith Hospital,
London W12 0HS

Hyperthermia, given alone or in combination with radiotherapy, is already being used to treat cancer patients who are not expected to respond favourably to conventional treatment. In particular, recurrent tumours at previously irradiated sites are being heated.

Experiments with rodents show that it is possible to separate two effects of heat. 1. Heating at temperatures greater than 41°C may cause direct thermal injury which is probably the result of intermitotic cell death. The severity of the reaction depends on both the temperature and duration of heating. 2. Heat treatments which alone cause little effect may enhance the response to radiation. In this case cells die at mitosis as is usual after ionizing radiations. Enhancement also depends on the temperature and duration of heating. It is maximal when heat and radiation are given simultaneously and decreases as the time between the two modalities is increased. Experiments using rodents show that if heat is given four to six hours after X rays, thermal enhancement is completely lost in normal tissues but not in tumours. Therefore a therapeutic gain may be achieved.

The long-term effect of a previous course of radiation on the reponse to hyperthermia has been investigated in two normal tissues of the mouse. Thermal sensitivity of the skin was increased at three to four months after X rays. Comparable increases in sensitivity to retreatment with X rays have been seen. Thermal sensitivity of the intestine was increased at two to three weeks after X rays, but in this case sensitivity returned to normal by four to five months.

There is no indication that patients who have received a previous course of radiotherapy are more sensitive to subsequent treatment by hyperthermia, either given alone or combined with radiation, than those who have had no previous treatment. However, only a small number of patients is available for review. The data from experiments using mice indicate that the possibility of increased thermal sensitivity after previous radiotherapy cannot be excluded.

CLINICAL ASPECTS OF RETREATMENT

By R. D. Hunter

Christie Hospital and Holt Radium Institute, Withington,
Manchester

Clinical teaching and instinct inhibit the practising radiotherapist from retreating malignant disease of "limited sensitivity" when recurrence has taken place within the previously treated volume. Tolerance has been considered to be exhausted in the first radical treatment and there is doubt about the responsiveness of recurrent or radiation induced tumours.

Personal experience of retreating heavily irradiated human skin and radiation-induced hypo-pharyngeal carcinoma had suggested that, after a gap of 20–40 years, tolerance in treated tissues recovers sufficiently to allow radical treatment to be given. Acute reactions are of normal severity and among 21 treated patients no necrosis was seen even when eight patients survived two years. In three patients the radiation-induced carcinoma proved radiocurable (Hunter and Stewart, 1977).

Reported international experience of retreatment of the primary volume after previous radical radiotherapy is limited. A critical review of the results obtained in retreating carcinomas of the larynx, pharynx and mouth has substantiated the previous experience of normal acute reactions following the second treatment. Late reactions with necrosis have been seen in anything up to one third of patients and appear more likely if the recurrence appears early, is of large volume or is treated by interstitial or intracavitary therapy. Late recurrence of carcinoma is controllable for periods of years. Clinical experience supports the concept of recovery of radiation tolerance with time in human tissues. The time scale of the process is not clear from the relatively random reported clinical events. There is no evidence to support the concept that a tumour recurrent after radical radiotherapy is likely to be radioresistant.

REFERENCE

HUNTER, R. D. and STEWART, J. G., 1977. The tolerance to re-irradiation of heavily irradiated human skin. *British Journal of Radiology, 50,* 573–575.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 36 Portland Place, London W1N 3DG.

Fellowships and Grants for Cancer Research

The International Union against Cancer invites applications for Yamagiwa-Yoshida Memorial International Cancer Study grants (deadline December 31) and International Cancer Research Technology Transfer Programme Grants. Details and application forms from: UICC, rue du Conseil-General 3, 1205 Geneva, Switzerland.

The International Agency for Research on Cancer (World Health Organization) invites applications for training fellowships in 1982/3 from junior scientists wishing to be trained in the fields of epidemiology, biostatistics and environmental carcinogenesis (both chemical and viral). Details and application forms from: The Head of the Research Training and Liaison Programme, 150 cours Albert-Thomas, 69372 Lyon Cedex 02, France. Deadline January 31 1982.

The Radiological Diagnosis and Treatment of Thyroid Disease

Wednesday, November 18, 1981

This all-day meeting, organized by the BIR Nuclear Medicine Committee, will be held at the Institute, 36 Portland Place, London W.1. The meeting will cover all aspects of thyroid disease, including the use of isotopes.

Subcellular Targets Including Ultrasonic Damage

Radiobiology Work-in-Progress all-day meeting, Friday, November 20, at 10.30 a.m. at 36 Portland Place, London W1N 3DG. BIR members £1, non-members £2. Enquiries to the General Secretary, The British Institute of Radiology, at the above address (telephone 01-580 4085).

The Royal College of Radiologists
46th Skinner Lecture on Measurement and Management of Cancer of the Breast

Dr. R. H. Thomlinson will deliver this lecture on Friday, November 20 at 4.30 p.m. at 66 Portland Place, London W1N 4AD. Chairman: Dr. John W. Laws, M.B., Ch.B., F.R.C.P., President of the College. Open to all members of the medical profession, free of charge. No tickets needed.

The Effects of Small Doses—the Basis of Radiation Protection

All-day meeting on Saturday, November 21, at 10.45 a.m., at 36 Portland Place, London W1N 3DG. Admission free. Chairman: Prof. R. J. Berry. Enquiries to the General Secretary, The British Institute of Radiology, at the above address (telephone: 01-580 4085).

The Royal College of Radiologists
Postgraduate Weekend Courses

Details of the above courses in Diagnostic Radiology and Radiotherapy & Oncology, to be held on Saturday, November 21, 1981, can be obtained from the Meetings Secretary, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG (telephone 01-636 4432/3).

Interventional Arteriographic Procedures

At the BIR, 36 Portland Place, London W1N 3DG, on Thursday, November 19 at 7.15 p.m. Speakers: Drs. D. J. Allison, M. Collins and D. Cumberland. Preceded (5.45 p.m.) by a State of the Art Seminar on "ERCP: the radiologist's approach" (Chairman: Dr. M. I. Lavelle).

Safety Review and Inspection of Nuclear Power Plants

The International Atomic Energy Agency will hold a seminar in Vienna from November 23-27, 1981. Further information and participation forms from D. A. Herbert, Department of Energy, Atomic Energy Division, Thames House South, Millbank, London SW1P 4OJ (phone 01-211 6850).

Combined Modality Therapy—Clinical and Laboratory Aspects

A joint meeting (British Institute of Radiology and British Association for Cancer Research) will be held on November 26 and 27 at The Royal College of Surgeons, Lincoln's Inn Fields, London. Speakers: Professor N. M. Bleehan, Drs. R. Sandland, L. L. Gunderson, W. H. Shipley, J. Overgaard, S. Dische and Professor P. Alexander (the 2nd Gordon Hamilton-Fairley Memorial Lecture). Enquiries to: Dr. M. J. Embleton, Cancer Research Campaign Laboratories, University of Nottingham, University Park, Nottingham NG7 2RD.

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14-15 at the University of London Union, Malet Street, London WC1.

British Association of Clinical Anatomists

The Annual General Meeting will take place at the Warwickshire Postgraduate Medical Centre, Stoney Stanton Road, Coventry on Friday, January 15, 1982.

Further details about the Association may be obtained from Prof. D. B. Moffat, Department of Anatomy, University College, P.O. Box 78, Cardiff CF1 1XC.

Quantities and Units for use in Radiation Protection

Scientific meeting and exhibition, National Physical Laboratory, Teddington, Middlesex, Tuesday, January 26, 1982. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

The Mayneord Symposium

Friday, February 19, 1982. This meeting is being organized by, the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. It will be an all-day meeting to be held at the Royal Society, 6 Carlton House Terrace, London SW1. The theme for the meeting will be "The future in radiology" as seen by distinguished workers in a number of branches of radiological science.

The Natural Radiation Environment

Tuesday, March 30, 1982, at the Central Electricity Generating Board, Sudbury House, 15 Newgate Street, London EC1. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Forthcoming events and notices

7th International Intensive Course in Abdominal Ultrasound

Besançon, France, April 14–16, 1982. Topics: technology, echoanatomy, sonography of the liver, biliary tract; pancreas, jaundice, spleen, urinary tract, retroperitoneal compartment, abdominal abscesses and fluid collections, acute and post-operative abdomen; obstetrics and gynaecology; guided biopsy. Practical training on sonograms and real-time videotapes. Faculty: Prof. F. Weill, Drs. Bihr, Le Mouel, Schraub, Rohmer (Besançon), Eisencher (Vesoul), Profs. Boog (Brest), Winsberg (Montreal), Curatti (Geneva), Holm (Copenhagen) and Dellenbach (Strasbourg). Registration limited to 150 participants. Write: Cours U.S., Secretariat, Départment de Radiologie viscérale (Prof. Francis Weill), 2 Place St. Jacques, CHU Besançon 25000, France.

European Society of Pediatric Radiology
19th Congress, Prague, April 22–24, 1982

Organized by the European Society of Pediatric Radiology, Czechoslovak Medical Society J. E. Purkyně, Czechoslovak Radiologic Society and the Czechoslovak Pediatric Society. Deadline for applications and abstracts: December 30, 1981. Information: Czechoslovak Medical Society J. E. Purkyně, 19th Congress of the European Society of Pediatric Radiology, Vítězného února 31, 120 26 Praha 2, Czechoslovakia.

Society for Radiological Protection
Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ.

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on The contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A. M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

5th South African International Radiological Congress

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas participants, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

7th International Congress of Radiation Research

Will be held at the International Congress Centre RAI, Amsterdam, The Netherlands, July 3–8, 1983. Information: Dr. J. J. Broerse (Secretary-general of the 7th ICRR), Radiobiological Institute TNO, PO Box 5815, 2280 HV Rijswijk, The Netherlands.

The British Journal of Radiology, September 1981

We apologise to all our readers for the lateness of the September issue.

Correspondence. 1009
Preset counts or preset time?
C. P. Wells, F. M. Hall, P. J. Mountford, A. J. Coakley; A. R. Constable and R. W. Cranage
Use of diagnostic ultrasound to measure the lumbar spinal canal.
A. Nachemson and M. Asztély; R. W. Porter
Radiation dose from human platelets labelled with indium -111.
O. R. van Reenen
Choosing between two formulations of a dose/cure function.
A. M. Walker and H. D. Suit; E. H. Porter

Erratum: A catheter system for tissue glues. 1013

Proceedings of The British Institute of Radiology. 1014
Thirty-ninth Annual Congress, April 9–10, 1981.

Forthcoming events and notices. 1025

Book reviews

Bone metastases 938
Cahiers de radiologie. 2. Le crâne 938
Multiple imaging procedures. 4. Urinary tract and adrenal glands 947
Radionuclide imaging artefacts 965
Gynaecological radiology 968
Radiation protection optimization 972
Environmental health criteria. 14. Ultraviolet radiation 972
Natural radiation environment. III 977
Ultrasonic tissue characterization 981
Clinics in diagnostic ultrasound. 4. Two-dimensional echocardiography. 5. New techniques and instrumentation 1008
Lecture notes in biomathematics 1013

Treatment Simulators

British Journal of Radiology Supplement 16, 1981

This is a revised version of a working-party report which was first published in 1976 as BIR Special Report 10, and owing to heavy demand has been out of print for some time. The authors consider the place of planning simulators in modern radiotherapy and endeavour to set up guide lines for their future development, covering both specifications for the instruments and the ways in which they are used. The report also discusses the relationship between simulators and transverse axial computed tomography.

The report has been fully updated and is highly detailed, containing 31 pages, 10 figures, and 59 references covering the period 1952 to 1981. The Convenor of the Working Party was C. K. Bomford and other members were Miss L. M. Craig, F. A. Hanna, G. S. Innes, S. C. Lillicrap and the late R. L. Morgan, with G. R. Higson as DHSS Observer.

Of practical interest to all involved with developments in radiotherapy.

ISSN 0306–2120 Price £3.50

Orders to:

Publications Department, The British Institute of Radiology,
36 Portland Place, London W1N 3DG
Tel: 01-580 4189 or through your bookseller.

VOL 54 NO 647 NOVEMBER 1981

The British Journal of Radiology

Contents

Page

Ultrasonography in acute cholecystitis. 927
F. Croce, G. Montali, L. Solbiati and G. Marinoni

Diaphyseal osteosarcoma. 932
J. M. Haworth, I. Watt, W. M. Park and J. Roylance

The chest radiograph in leptospirosis in Jamaica. 939
R. E. J. Lee, S. I. Terry, T. M. Walker and A. E. Urquhart

An assessment of intravenous urogram imaging using 100 mm and conventional films. 944
Elizabeth M. Robertson, B. Baily, Tamarisk M. Hearnden, R. F. Mould and D. H. Trapnell

Initial findings in the computer-aided diagnosis of cerebral tumours using CT scan results. 948
K. Wills, G. H. du Boulay and D. Teather

CT brain scans: part of a 20-year development study following gross undernutrition during infancy. 953
L. C. Handler, M. B. Stoch and P. M. Smythe

The role of abdominal computed tomography in lymphoma following treatment. 955
G. Blackledge, H. Mamtora, D. Crowther, I. Isherwood and J. J. K. Best

Dosimetry of renal radiopharmaceuticals: the importance of bladder radioactivity and a simple aid for its estimation. 961
T. Smith, N. Veall and D. G. Altman

The effect of photon absorption by breast tissue in myocardial imaging with thallium 201. 966
H. Singh and D. A. Causer

Modification of the oral radiation death syndrome with combined WR-2721 and misonidazole. 969
P. Grigsby and Y. Maruyama

Repair of sublethal and potentially lethal damage in lung cells using *in vitro* colony method. 973
P. J. Deschavanne, Marcelle Guichard and E. P. Malaise

Technical note. 978
The accuracy of dimensional measurement in ultrasonic real-time scanning.
R. C. Chivers, R. A. Bacon and T. J. Bloomberg

Case reports. 982
Hippel-Lindau syndrome in identical twins.
D. P. Wesolowski, R. A. Ellwood, R. E. Schwab and J. Farah
An intracardiac foreign body: diagnosed non-invasively and removed non-surgically.
J. Davies, R. Alvares and D. J. Allison
Cementifying fibroma (so-called "cementoma") of tibia.
J. J. Kolar, V. Horn, H. Zidkova and J Sprindrich
Metastatic disease to the carpus.
P. C. Cary, C. A. Helms and H. K. Genant
Hypothenar hammer syndrome.
D. R. Foster and D. C. Cameron
The importance of radiological monitoring after oesophageal intubation.
W. B. Campbell and D. J. Mackenzie-Crooks
Recurrent gall-stone ileus.
A. U. Haq, A. H. Morris and H. Daintith
Osteoblastic metastases in renal cell carcinoma.
A. I. Neugut, E. S. Casper, T. A. Godwin, and Julius Smith
Second primary neoplasm in a dysgerminoma patient.
O. M. Koriech and G. H. D. McNaught

Short communication. 1006
Mechanism of misonidazole-linked cytotoxicity and altered radiation response: role of cellular thiols.
J. E. Biaglow, Marie E. Varnes, M. Astor and E. J. Hall

(*continued on inside back cover*)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by The British Institute of Radiology
36 Portland Place, London W1N 3DG

ISSN 0007-1285
17249

14.9.82

Volume 54 Number 648
December 1981

THE BRITISH JOURNAL OF RADIOLOGY

[illegible]

and related [illegible]

Published by
The British Institute of Radiology

The British Journal of Radiology

Founded 1896

The Editorial Committee consists of:

The Editors:

J. L. Haybittle, M.A., PH.D. J. Roylance, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. Hale, M.B., CH.B., F.R.C.R., D.M.R.T. A. B. Ayers, M.D., D.M.R.D., F.R.C.R.
N. J. McNally, B.SC., M.SC., PH.D.

and

The Associate Editors:

Thelma D. Bates, M.B., CH.B., F.R.C.R., D.C.R.A.
D. Cosgrove, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. Cottrall, B.A., M.SC., PH.D., F.INST.P.
J. C. W. Crawley, B.SC., C.ENG., M.I.E.E.
R. Dick, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. Flower, M.A., F.R.C.P.(C.), F.R.C.R.
J. A. Gleeson, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. Gravelle, B.SC., M.B., CH.B., F.R.C.P.(E.), F.R.C.R., D.M.R.D.
C. H. Jones, B.SC., PH.D., F.INST.P.
D. H. Keeling, M.A., M.SC., M.B.
I. Kelsey Fry, D.M., F.R.C.P., F.R.C.R.
B. Kendall, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. Meire, M.B., B.S., L.R.C.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
J. T. Patton, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. Perry, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. Savage, D.SC.
P. N. T. Wells, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. Armstrong, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. Cohen, PH.D., F.INST.P. (North America)
B. J. Cremin, F.R.C.R., F.R.A.C.R. (South Africa)
R. Fox, D.PHIL. (Australia)
H. A. Luke, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. Sim, M.B., CH.B., F.R.C.R., F.R.A.C.R. (New Zealand)
D. M. Taylor, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: Mrs. L. F. Secretan, M.A.

Communications should be addressed to the Editors in accordance with the Instructions to Authors which are published in the January issue of the Journal in each year and copies of which may be obtained on application to the Managing Editor.

Advertisements: Communications regarding accounts should be addressed to the Institute. All other communications should be addressed to Miss Jean Somerville, Advertising Manager, The British Journal of Radiology, Advertisement Department, 24a Litchfield Street, London WC2H 9NX (01–836 5281).

Subscriptions: All communications should be sent to The British Institute of Radiology, 36 Portland Place, London W1N 3DG, England. Notification of change of address should include an old mailing label and the new address. Claims for missing copies can only be allowed if received within two months of normal delivery date.

Annual Subscription: (post free) £55·00 per annum, payable in advance (USA, $146). Single copies: £6·00 (USA, $14). (From January 1, 1982: £65·00 ($145), single copies £7·00 ($16); postage extra on all orders received after April 30, 1982.)

Second class postage paid at New York. Mailing agents N.Y.: Expediters of the Printed Word Ltd., 527 Madison Avenue, Suite 1217, New York N.Y., 10022, U.S.A.

The British Institute of Radiology

Incorporated by Royal Charter
Patron: Her Majesty The Queen

Founded 1897
36 PORTLAND PLACE, LONDON W1N 3DG
Telephone: 01–580 4085 and 580 4189. Cable Address: "Britology, London W.1."

President: M. J. Day, B.A., PH.D.

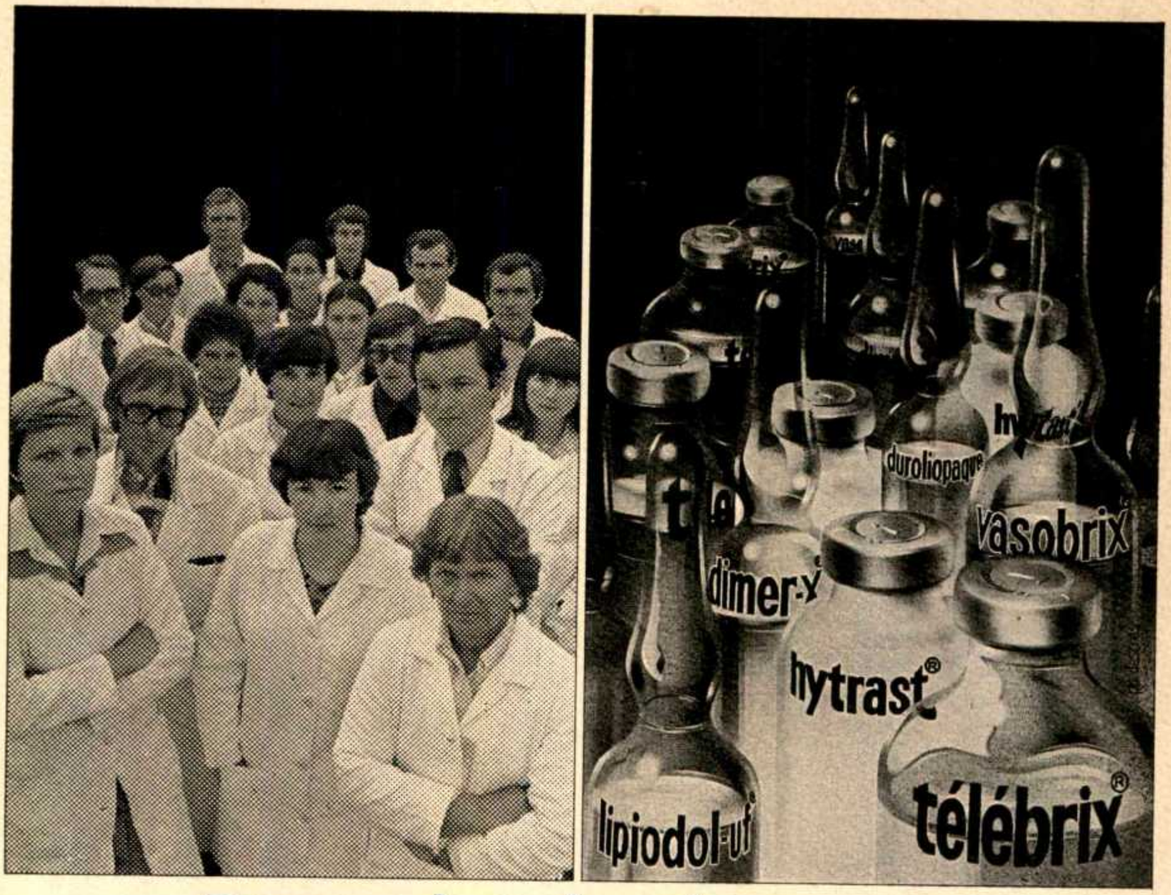
Hon. Secretaries:
M. F. Cottrall, B.A., M.SC., PH.D., F.INST.P.
Janet Husband, M.R.C.P., F.R.C.R.

Hon. Treasurer: D. Pace

General Secretary: Mrs. J. Royston

The British Institute of Radiology is an association of persons interested in Radiology and allied subjects. Meetings are held monthly from October until May. Particulars of membership and other information may be obtained on application to the General Secretary at the Institute.

© The British Institute of Radiology, 1981



Research & development

GUERBET

Better contrast media through research

Laboratoire GUERBET
16-24, rue Jean Chaptal - 93601 Aulnay-sous-Bois - Cedex FRANCE
Tél.: 866.78.37 - Télex: 212382 F.

New From
BAILLIÈRE
TINDALL

A GUIDE TO RADIOLOGICAL PROCEDURES

Stephen Chapman MB BS MRCP Department of Radiodiagnosis, Bristol Royal Infirmary; Tutor in Radiodiagnosis, University of Bristol

and

Richard Nakielny MA BM BCh Department of Radiodiagnosis, Bristol Royal Infirmary; Tutor in Radiodiagnosis, University of Bristol

with contributions by

W.D. Jeans FRCR Consultant Radiologist, Bristol Health District; Senior Lecturer in Radiodiagnosis, University of Bristol.

Foreword by
J.H. Middlemiss CMG MD FRCP FRCS FRCR

This book provides the basic information on radiological procedures required for Part 1 of the Fellowship of the Royal College of Radiologists and similar examinations in several overseas countries. The text is laid out in a manner appropriate to the examination requirements and the concise style enables the reader to obtain the information rapidly. Useful notes are included on some of the more sophisticated techniques that the trainee radiologist may encounter.

The book will also be of value to radiographers preparing for higher examinations and for junior hospital doctors faced with the ever-increasing complexity of radiological procedures.

1981 · 250 pages 8 tables · £6.50

BAILLIÈRE TINDALL
35 Red Lion Square, London WC1R 4SG

All details are subject to change without notice.

University and Hospital Departments of Radiology of Leeds and Sheffield

F.R.C.R. Preparation Course 1982

A three day Course organised jointly by the Departments of Radiology of Leeds and Sheffield and specifically designed to prepare candidates for Part II F.R.C.R. examination will be held at Sheffield, February 25, 26 and 27, 1982.
A subsequent complementary three day Course will be held in Leeds on September 7, 8 and 9, 1982. Separate registration necessary. Each course will consist of review lectures, M.C.Q. and written questions, tutorials and viva voce examinations.
Course fee for Sheffield program—£75.00 including luncheons. Residential accommodation available at an additional fee of £55.00.

Application forms and further details from :-
Post-graduate Medical Education Section,
Trent Regional Health Authority,
Fulwood House,
Old Fulwood Road,
Sheffield S10 3TH

Places strictly limited to 32 registrants for each course. Early application essential.

Co-ordinators—Dr. R. G. Grainger, Royal Hallamshire Hospital, Sheffield S10 2JF
—Dr. W. P. Butt, St. James's Hospital, Leeds LS9 7TF

BOMBAY INDIA

Applications are invited for the post of :-

CONSULTANT RADIOLOGIST

on a full-time basis for the
Jaslok Hospital & Research Centre.

The post would be that of Senior Consultant (full time) reporting directly to the Medical Director of the Hospital.
Responsibility will be for 3 to 4 imaging systems covering Neuroradiology and Whole Body CT Scanning.
All Radiographers and non-technical staff in the department will report directly to the successful applicant.
Three years experience of CT scanning and preferably some experience of rotate technology Scanners is sought.

In addition, applications are invited for the position of
CT Scanner Specialist Radiologist
reporting to the Consultant Radiologist. Recent CT experience is essential.

Applications in writing giving brief personal details, qualifications and availability should be sent to :-
Chanrai International Ltd.,
29/37 Norton Folgate,
London E.1
Tel No. (01) 377 8088
Attention :- Mr. V. H. Mirchandani

for the treatmen of malignant effusions

Coparvax is a freeze-dried preparation of Corynebacterium parvum. When injected into previously-aspirated pleural or peritoneal effusions, Coparvax has been shown to be extremely effective at preventing recurrence and easing the associated symptoms.

In addition, Coparvax has a remarkably low incidence of side-effects, unlike many other treatments, some of which may require concomitant narcotic analgesia.

For further information on this advance in the management of malignant effusions please contact our Scientific Services Division at the address below.

PRESCRIBING INFORMATION

Presentation Vial containing 7mg (dry weight of the inactivated *Corynebacterium parvum* organisms WFL strain CN 6134) with thiomersal, in a freeze-dried form. **Uses** Alleviation of malignant pleural effusions and malignant ascites. **Dosage** 7-14mg recommended, although some patients have responded to lower doses. **Administration** Freeze-dried Coparvax should be reconstituted with 1ml of physiological saline for injection and diluted in a further volume of 10-20ml prior to injection. The suspension should be injected, within 24 hours of reconstitution, into the pleural or peritoneal cavity via the paracentesis needle immediately after the effusion has been aspirated. Injection may be repeated, if necessary, at intervals of one to four weeks. **Contra-indications** During pregnancy, and patients with known hypersensitivity to thiomersal. **Precautions** The incidence and severity of side-effects attributable to Coparvax administered intrapleurally, appears to be intensified if given within 10 days of thoracotomy and lung resection probably due to enhanced systemic absorption of Coparvax. Coparvax should not be given during the immediate post-operative period. Following intrapleural or intra-abdominal administration, leakage of Coparvax into subcutaneous tissues may result in local tenderness. Intense fibrinous reaction in the pleural and peritoneal cavities has been observed following local administration of Coparvax. Intestinal obstruction due to the formation of adhesions is a theoretical possibility, although it has not been reported as a complication of Coparvax administration. **Adverse effects** Fever occurs in 10 to 40% of patients following intracavitary injection. Abdominal pain or mild abdominal discomfort has been reported in some 20% of patients following intraperitoneal instillation. Nausea and vomiting may occur in a minority of patients following intracavitary administration of Coparvax. **Basic NHS Cost** Single vial (7mg), £30 (PL3/0097).

Coparvax*

Corynebacterium parvum

when the quality of life is the primary concern

Calmic Medical Division
The Wellcome Foundation Ltd.
Crewe, Cheshire
(Tel: 0270 583151)

*Trade Mark

It's in the bag...

E-Z-EM ®

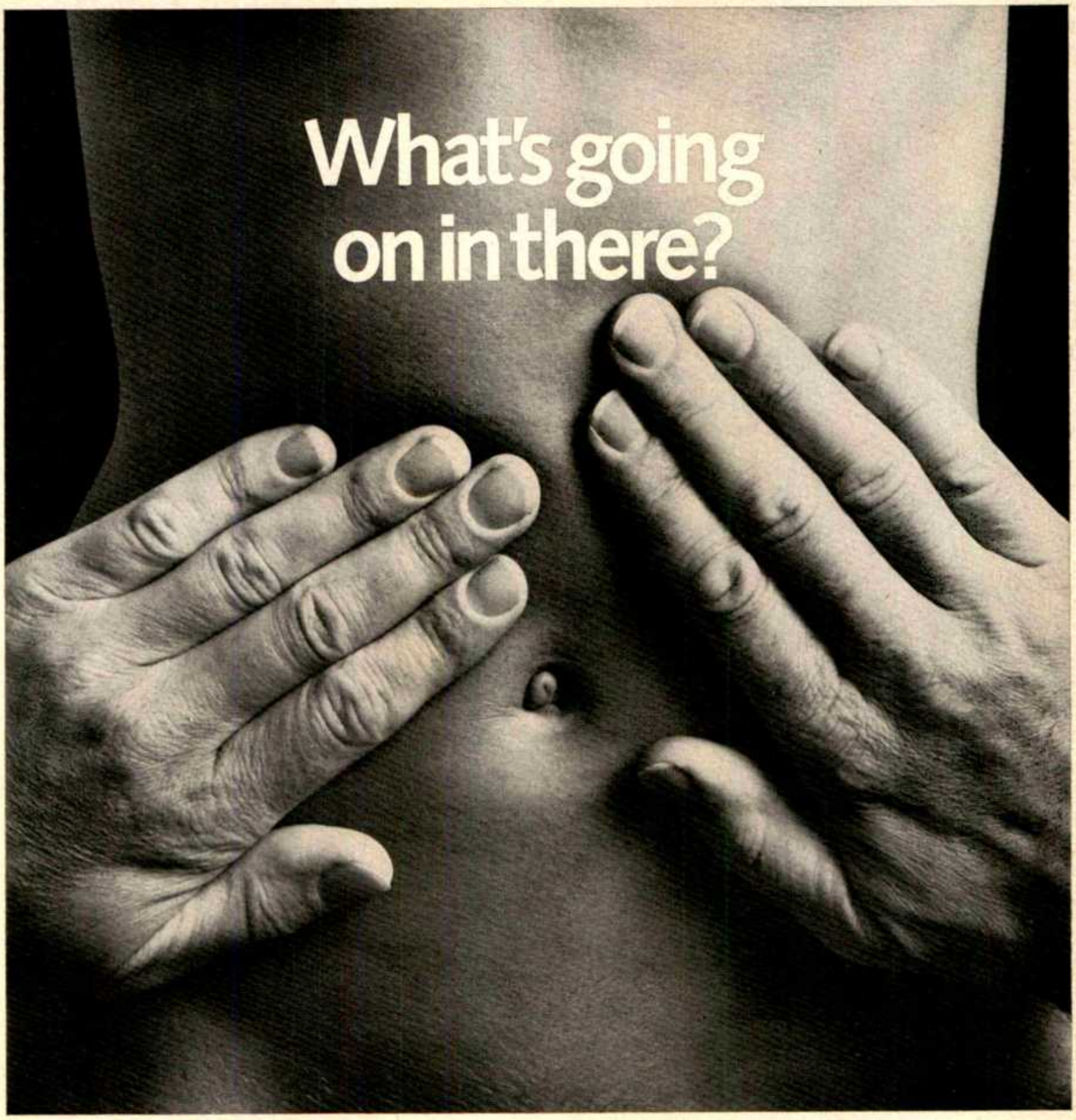
The complete disposable barium enema kit.

Full details from:

Henleys Medical Supplies Ltd. London N8 0DL Tel: 01-889 3151

PL/1665/0001

Produced by E-Z-EM Ltd London


What's going on in there?

Trust baritop to tell you

Baritop contrast medium: high density and low viscosity to give smooth and even coating of the GI tract, time after time. The special consistency of Baritop makes the most of your double-contrast technique.

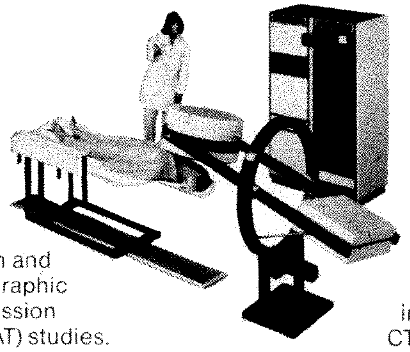
Baritop 100 ready-made suspension in ring-pull can for easy use. Baritop G powder for higher density. Baritop gas producing effervescent tablets complete with defoaming agent.

baritop excellent resolution every time

Concept Pharmaceuticals Ltd.,
59-61 High Street, Rickmansworth, Herts. WD3 1EZ. Tel. Rickmansworth (09237) 79388.

Which company offers a complete nuclear diagnostic ECAT system?

General Electric Company of U.S.A:*
Keeping you ahead of changing technology.



From one source — General Electric of U.S.A. — you can get both the MaxiCamera 400T nuclear camera system and a data processor with tomographic software for performing Emission Computed Tomography (ECAT) studies.

Because they were designed for each other — not acquired and put together from different suppliers — you get maximum performance from both; providing, for example, an added diagnostic dimension for visualising the liver, brain and heart.

Emphasis on advanced technology extends to other systems as well. In multi-axis vascular imaging, General Electric of U.S.A. combines the state-of-the-art Fluoricon L300 imaging system with fully compatible digital fluorography to meet growing diagnostic and therapeutic needs; in computed tomography, CT/T system technological advances include Dynapak expanded dynamic scanning, Arrange reformatting capability and nominal 1.5 mm slice thickness; in ultrasound, Datason system with real time sector scanning optimizes acoustic access for enhanced visualisation of anatomy.

Advanced imaging technology. One more reason why General Electric of U.S.A. is a significant and rapidly growing factor in European health care.

At the leading edge of imaging technology.

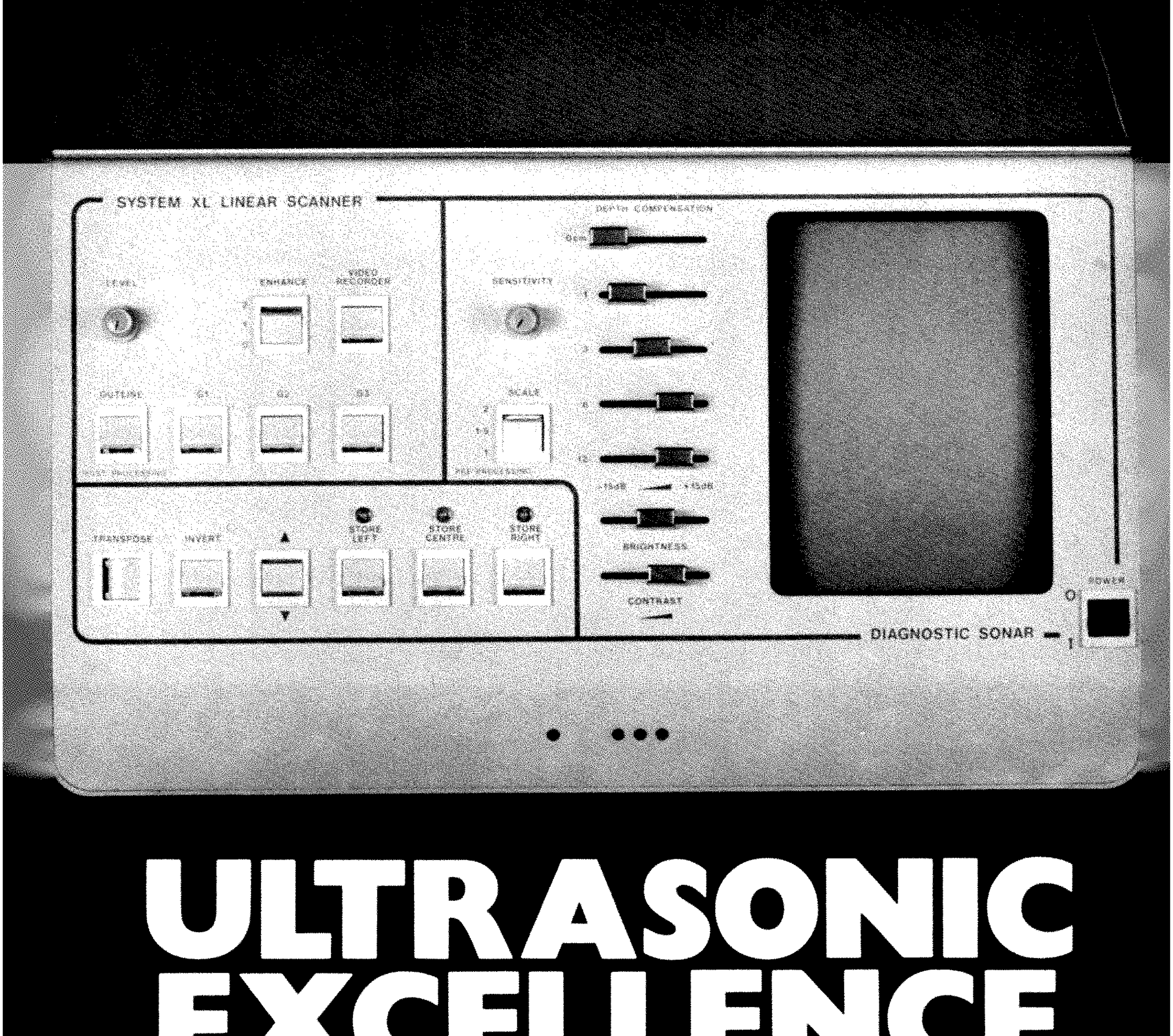
Frankfurt/M. Tel.: 06 11/7 60 73 69 • Wien, Tel.: 24 14 51 • Brüssel, Tel.: 660 2010 • Kopenhagen, Tel.: 2 86 86 00 • Mailand, Tel.: 753 1351 • Breda, Tel.: 76 22 54 15 • Lissabon, Tel.: 36 71 55 • Madrid, Tel.: 252 5100 • Goteborg, Tel.: 42 09 70 • Zürich, Tel.: 47 50 30

International General Electric Company of New York Ltd.,
Jubilee House, Blyth Road, Hayes, Middlesex. Tel: 01-573 7766.

GENERAL ELECTRIC
U.S.A.

*General Electric Company of the U.S.A. is not connected with the English company of a similar name.

SYSTEM XL



ULTRASONIC EXCELLENCE
IN REAL TIME LINEAR SCANNERS

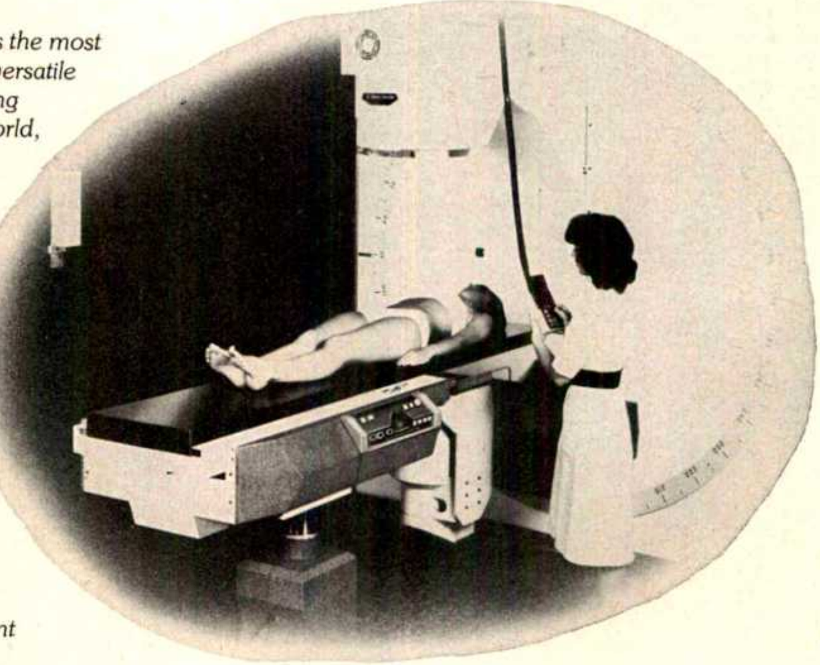
DIAGNOSTIC SONAR

Baird Road, Kirkton Campus, Livingston EH54 7BX, Scotland
Telephone: 0506 411877. Cables: Sonar Livingston. Telex: 72591 DSONAR G.

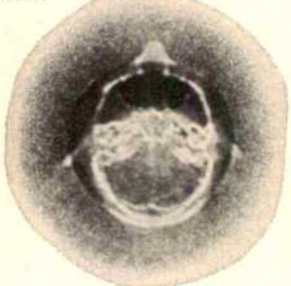
T E M

Ximatron 5
Treatment Planning Simulator

The Ximatron 5 is the most accurate and versatile treatment planning unit in the world, and the product of over fifteen years of simulator development and manufacture.

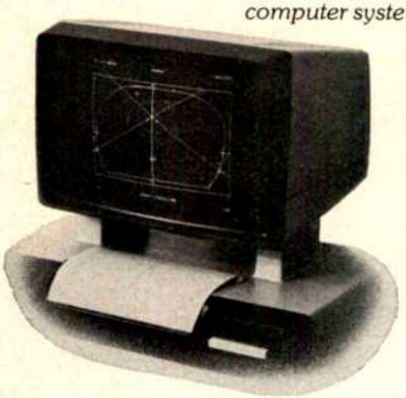


Forever mindful of the future, T.E.M. have incorporated the Ximascan into the Ximatron 5. This facility allows a digital tomographic scan of the patient to be taken.



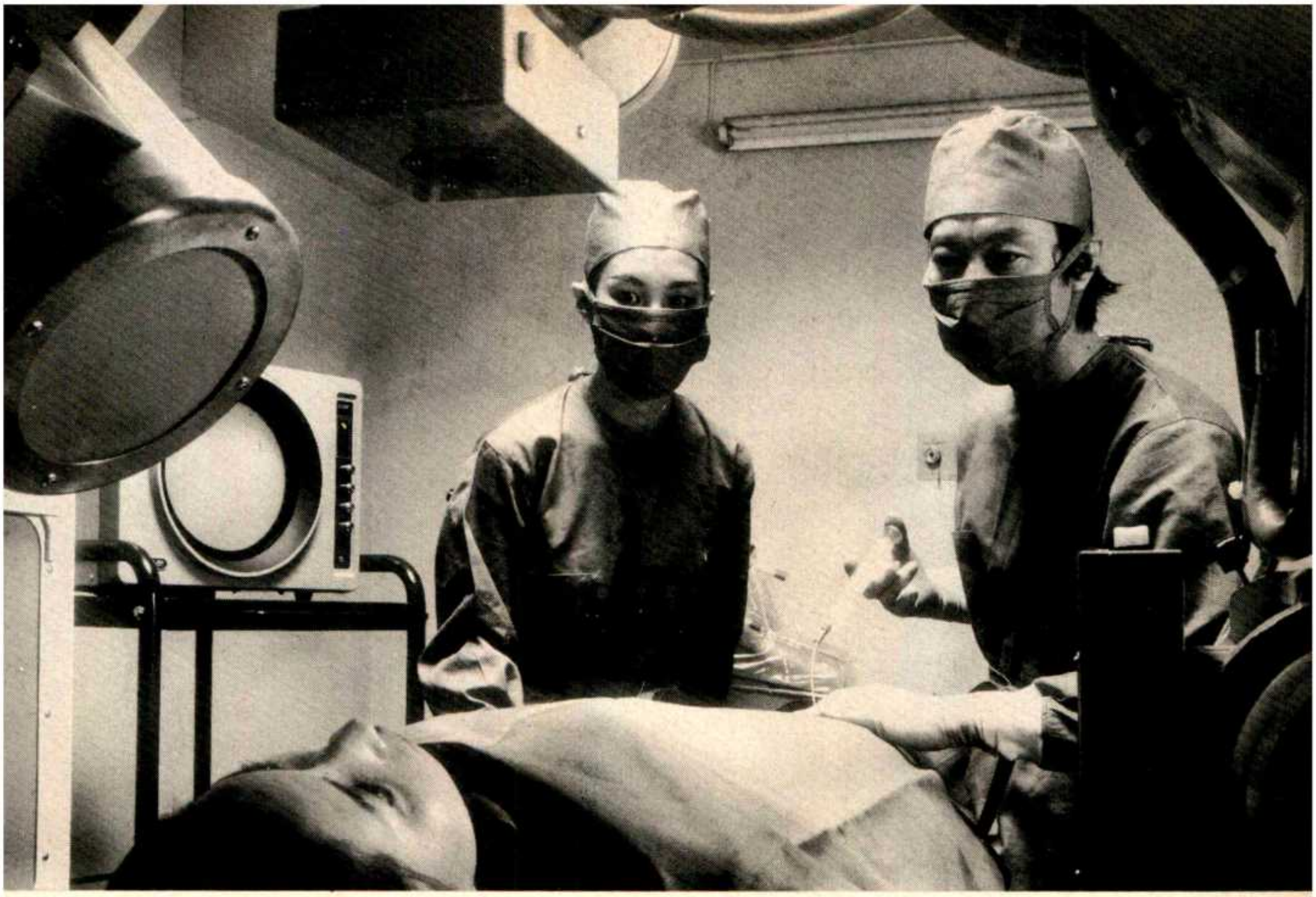
Variable speed controls facilitating quick and easy setting and planning procedures, providing digital readouts with a B.C.D. output.

The Ximascan may be interfaced directly to the T.E.M. treatment planning computer system.



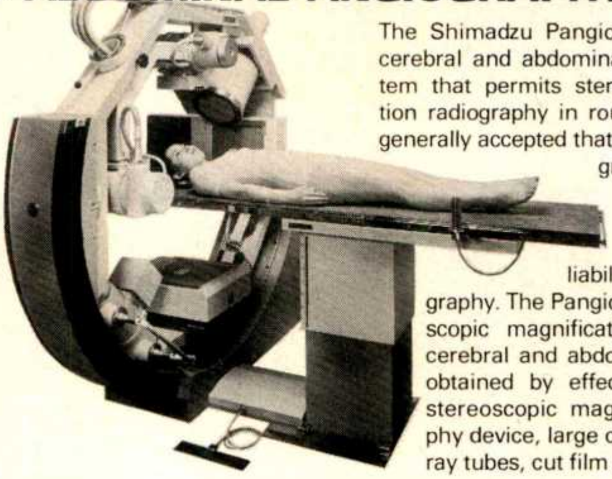
For further details:

TEM Instruments Limited
Gatwick Road, Crawley, Sussex, RH10 2RG, England Tel 0293 31244
Telex: 87397, Grams: TESTMENT CRAWLEY



PANGIOMAX

CEREBRAL AND ABDOMINAL ANGIOGRAPHY SYSTEM



The Shimadzu Pangiomax is a dedicated cerebral and abdominal angiographic system that permits stereoscopic magnification radiography in routine diagnosis. It is generally accepted that magnification radiography and stereography effectively increase the diagnostic reliability of cerebral angiography. The Pangiomax permits stereoscopic magnification images of the cerebral and abdominal vessels to be obtained by effectively combining a stereoscopic magnification radiography device, large capacity fine-focus x-ray tubes, cut film changers, etc.

SHIMADZU
CORPORATION KYOTO JAPAN

INTERNATIONAL MARKETING DIV.
Shinjuku-Mitsui Building, 1-1, Nishishinjuku 2-chome, Shinjuku-ku, Tokyo 160, Japan
Phone: Tokyo 03-346-5641 Overseas Telex: No. 0232-3291 SHMDT J.
SHIMADZU (Europa) GmbH
4000 Düsseldorf 1, Johannes Weyer Str. 1 F.R. Germany
Phone: (0211) 314061 Telex: 08586839 SHIM D.
MEDICAL X-RAY SUPPLIES LTD.
Cottrell House 53-63 Wembly Hill Road, Wembly, HA9 7PR
Phone: 01-902-6098 ENGLAND

University of London
British Postgraduate Medical Federation

CARDIOTHORACIC INSTITUTE at Brompton Hospital

COURSE IN PULMONARY RADIOLOGY 17th–19th February 1982

This course is designed particularly for Senior Registrars in radiology studying for the final F.R.C.R. examination.
Topics will include

- Techniques
- Infection and Trauma
- Pulmonary Infiltration
- Neoplastic Disease
- CAT Scanning
- Paediatric Radiology
- Obstructive Airways Disease

Programme includes lectures and tutorials

Fee: £95 including hospitality

Application forms available from Dean's Office,
Cardiothoracic Institute, Fulham Road, London SW3 6HP.
(Tel: 01-352 8121 Ext 4187)

UNIVERSITY OF NIGERIA, NSUKKA

STAFF VACANCIES

Applications are invited from suitably qualified candidates for the following staff vacancies :-

A. ACADEMIC STAFF

1. DEPARTMENT OF RADIATION MEDICINE
   Advert. Ref. : UNP/SSR.9/RAD/ACAD/981
   Posts : (a) Senior Lecturer I (b) Lecturer I (Radiodiagnosis)

Qualifications & Experience

1. Senior Lecturer Grade I: Specialist degree registrable by the Nigerian Medical Council (by DMRD FFR) plus at least seven years post-qualification relevant teaching or research experience and reasonable number of scholarly publications.
2. Lecturer I: As for Senior Lecturer Grade I but in relevant field and with at least three years relevant post-qualification experience.

B. FOR NON-ACADEMIC VACANCIES

DEPARTMENT OF RADIATION MEDICINE
Advert. Ref. : UNP/SSR.9/RAD/981
Post : Chief Principal Radiographer
Duties will include Radiography, Ultrasonography and field work.
Qualifications & Experience : A recognised certificate in Radiation Protection and a Diploma of the College of Radiographers (London) plus at least 8 years post-qualification experience for Chief Radiographer or 6 years for Principal Radiographer.

SALARY

Senior Lecturer I	GL.14 : N9,168 – N10,128 p.a.
Chief Radiographer	GL.13 : N8,064 – N9,024 p.a.
Lecturer I Principal Radiographer	GL.12 : N7,404 – N8,052 p.a.

Point of entry will depend on qualification and experience. A clinical supplementation of N3,000 p.a. is payable to medically qualified successful candidates.

CONDITIONS OF SERVICE:

For Nigerians, and non-Nigerians on contract, fare paid for appointee, wife and up to five children aged eleven years or under on appointment. Annual leave with leave allowance for Nigerian staff and three months vacation leave for every completed 21 months for non-Nigerian staff. Free medical service, part-furnished accommodation at standard rates, if available, or rent allowance paid in lieu. Appointment of expatriates is on CONTRACT for a specific period with a contract addition of 10 or 15 per cent of salary every month (whichever is applicable) and 15 per cent of terminal annual salary at the expiration of contract as gratuity for every year of service.

METHOD OF APPLICATION:

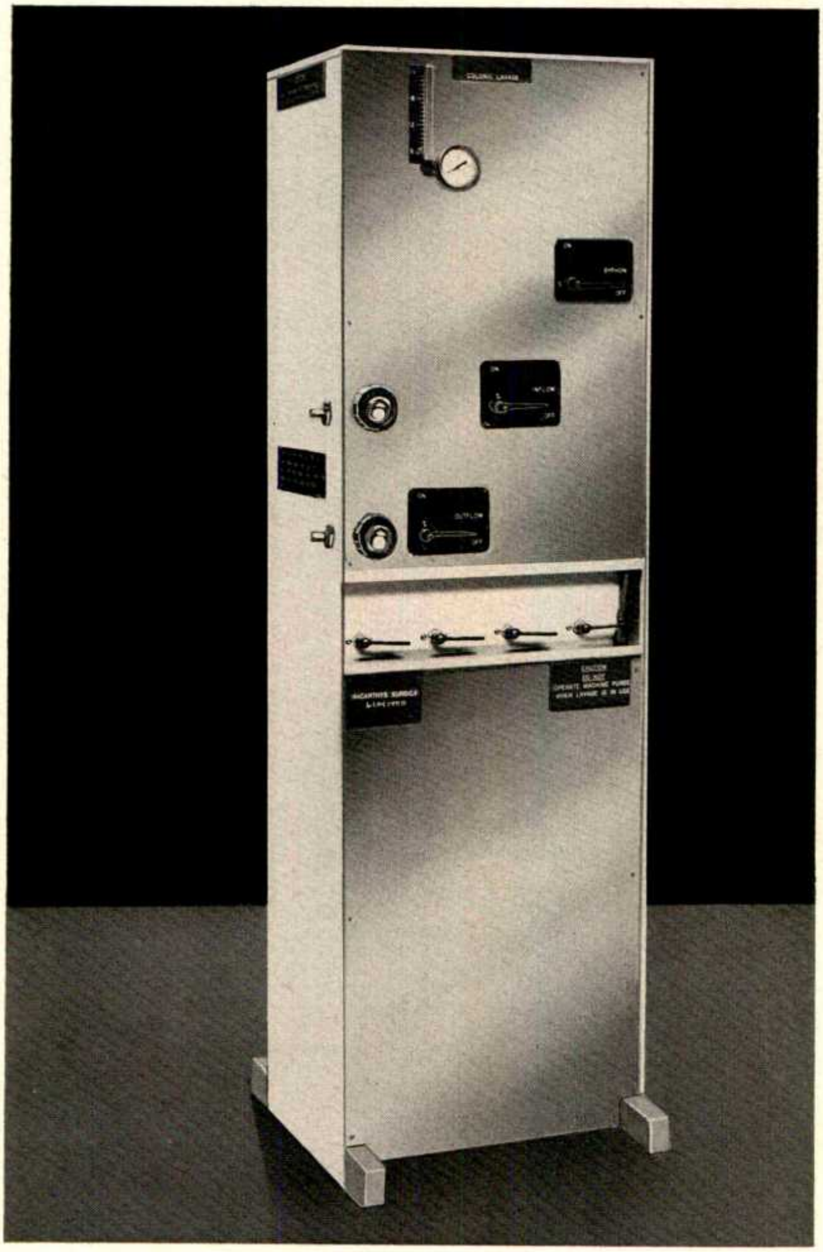
Send five copies of typewritten application and signed curriculum vitae stating nationality, age, marital status, details of educational and professional qualifications with specific dates, and addresses of three referees competent to attest to applicant's professional/academic ability to ACTING PERSONNEL OFFICER, UNIVERSITY OF NIGERIA, NSUKKA ,NIGERIA, and ONE COPY to the Principal Assistant Secretary (Recruitment), Nigerian Universities Office, 180 Tottenham Court Road, London W1P 9LE. Applicant should attach a photocopy of each relevant certificate claimed and inform his nominated referees of the post applied for and to forward sealed typewritten confidential reports on his behalf direct to the ACTING PERSONNEL OFFICER at the above address. Applications which do not comply strictly with the requirements of this advertisement will not be processed.

Candidates who had applied to us for the re-advertised vacancies need not to re-apply.

Staff in the Nigerian Public Service should channel their applications through their Heads of Department.

CLOSING DATE: 21 Days from the date of this publication.

HENDERSON
COLONIC LAVAGE UNIT



The Henderson Colonic Lavage provides a simple, effective and safe apparatus for washing out the large intestine and the terminal ileum of the small bowel.

The Henderson Colonic Lavage is indicated for patient preparation prior to surgery or radiography.

An important feature of this machine is, that as fluid is withdrawn from the patient, air is admitted to maintain the full lumen of the bowel, permitting complete fluid evacuation and assisting further faecal removal.

Macarthys Surgical Ltd

DAGENHAM
Selinas Lane
Dagenham, Essex RM8 1QD
Tel.: 01-593 7511

BIRMINGHAM
Unit 25/28
Edgebaston Shopping Centre
Hagley Road
Birmingham B16 8SH
Tel.: 021-454 6713

GLASGOW
301-3 Glentanar Road
Balmore Industrial Estate
Glasgow G22 7UG
Tel.: 041-336-8782

LIVERPOOL
201-3 London Road
Liverpool L3 8JS
Tel.: 051-207-1348

MANCHESTER
Precinct Centre
Oxford Road
Manchester M13 9GS
Tel.: 061-273-6754/5

HEYDEN HM + M PUBLISHERS LTD.

CROHN'S WORKSHOP

A Global Assessment of Crohn's Disease

Edited by Emanoel C.G. Lee
Consultant Gastroenterological Surgeon
John Radcliffe Hospital, Oxford, UK

An authoritative guide to the present status of Crohn's disease worldwide based upon the programme of the Cape Town Workshop. It presents an assessment of the modern endoscopic and radiological diagnostic techniques employed. Problems of diagnosis, the current mode of clinical presentation, and the changes that have taken place since the disease was first described are all reviewed.

ISBN0 85602 085 0 196pp 51illus. 41 tables
Casebound £16.50 Publication Oct. '81.

Sales and Distribution:
HEYDEN Heyden & Son Ltd., Spectrum House, Hillview Gardens, London NW4 2JQ.

ORDER FORM

Please complete the details below and return to Heyden & Son at the address given below:

Please send to me:

. . . . copy/copies of CROHN'S WORKSHOP ISBN 0 85602 085 0 £16.50

☐ A fully detailed prospectus

☐ The latest catalogue of HM+M Publications

☐ I enclose payment of . . . . . . / please bill me

CREDIT CARDS

For orders placed with Heyden's UK office we accept: Access/Barclaycard/American Express/Diners Club

☐ Please charge to my Credit Card account

Card No . . . .

Card Type . . . . Exp. Date . . . . . .

Name. . . . .

Organisation. . . . .

Address. . . . .

. . . .

Signature. . . . . Date. . . . .

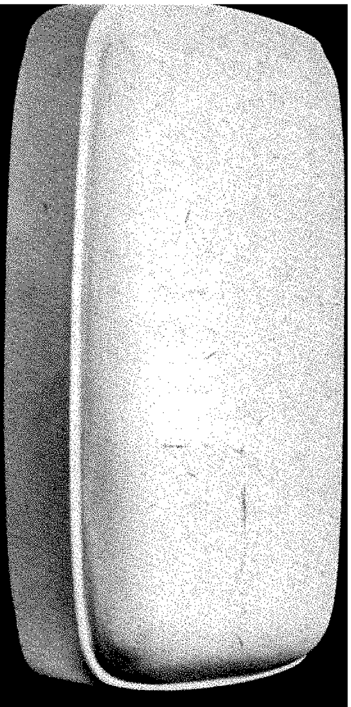
Didronel Prescribing Information

Presentation: White rectangular tablets containing etidronate disodium 200mg.
Indications: The treatment of Paget's disease of bone (osteitis deformans).
Effectiveness has been demonstrated primarily in patients with polyostotic Paget's disease with symptoms of pain and with clinically significant elevations of urinary hydroxyproline and serum alkaline phosphatase.
Dosage and administration: 5mg/kg/day to 20mg/kg/day as detailed below.
a) Adults: Usually 5mg/kg body weight/day, not to exceed a period of six months. Doses above 10mg/kg should be reserved for use when there is an overriding requirement for suppression of increased bone turnover associated with Paget's disease or when the patient requires more prompt reduction of elevated cardiac output. Doses in excess of 20mg/kg/day are not recommended.
Retreatment should be undertaken only after a drug-free period of at least three months and after it is evident that reactivation of the disease has occurred. In no case should duration of retreatment exceed the maximum duration of the initial treatment. Premature retreatment should be avoided.
b) Children: Juvenile Paget's disease, has been reported rarely. The relationship to adult Paget's disease has not been established.
c) Directions for use: Didronel should be administered as a single, oral dose, two hours before meals. It may be given with fruit juice or water. Eating should be avoided for two hours before and after drug administration to avoid reduced absorption.
Contraindications, Warnings, etc.
Contraindications: None demonstrated to date.
Precautions:
1. General
Extended periods of medication should be approached cautiously. When administered at doses of 20mg/kg/day, Didronel suppresses bone turnover and essentially stops mineralisation of new bone in Pagetic lesions and, to a lesser extent, in the uninvolved skeleton. Mineralisation of Pagetic lesions has been demonstrated to occur normally after discontinuation of the drug.
Patients with restricted vitamin D and calcium intake may be particularly sensitive to drugs that affect calcium homeostasis and should be closely followed while under treatment with Didronel.
Didronel is not metabolised but excreted intact via the kidney; therefore, treatment of patients with impaired renal function should be approached very cautiously, if at all.
Contraindicated in enterocolitis and for theoretical reasons in pregnant women and nursing mothers.
Warnings:
The physician should adhere to the recommended dose regimen. The response to therapy may be of slow onset and may continue even for months after treatment when the drug has been discontinued. Dosage should not be increased prematurely nor should treatment be resumed before there is clear evidence of reactivation of the disease process.
Retreatment should not be initiated until the patient has had at least a three-month drug-free interval.
There has been no evidence of increased risk of fractures at the recommended dose of 5mg/kg/day for six months. The risk of fracture may be increased when Didronel is taken at a dose level of 20mg/kg/day in excess of three months. This risk may be greater in certain patients. It is recommended that the drug be discontinued when fractures occur and that therapy not be reinstated until fracture healing is complete.
Pagetic lesions should be evaluated carefully to differentiate these from osteogenic sarcoma.
Side-effects: At doses greater than 5mg/kg/day, diarrhoea, loose bowel movement or nausea may occur.
Pharmaceutical precautions: Normal pharmaceutical storage and handling are indicated.
Legal category: POM.
Package quantities: 60 x 200mg tablets (Price £29.88).
Further information: Nil.
Product Licence Number: 0166/0101.

Brocades|Great Britain|Ltd.
West Byfleet, Weybridge, Surrey, KT14 6RA. Telephone: Byfleet 45536/42291

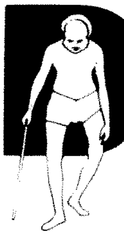
A Product of
Procter & Gamble Research

No.



THE FIRST SPECIFIC ORAL TREATMENT FOR PAGET'S DISEASE OF BONE

- ✻ Simple, once daily oral dosage.
- ✻ Symptomatic relief in over 60% of patients.
- ✻ Retards the disease in the majority of patients.
- ✻ Post therapy remission sustained from 3 months to 2 years.
- ✻ Low incidence of side effects.
- ✻ Less expensive than other specific therapies.



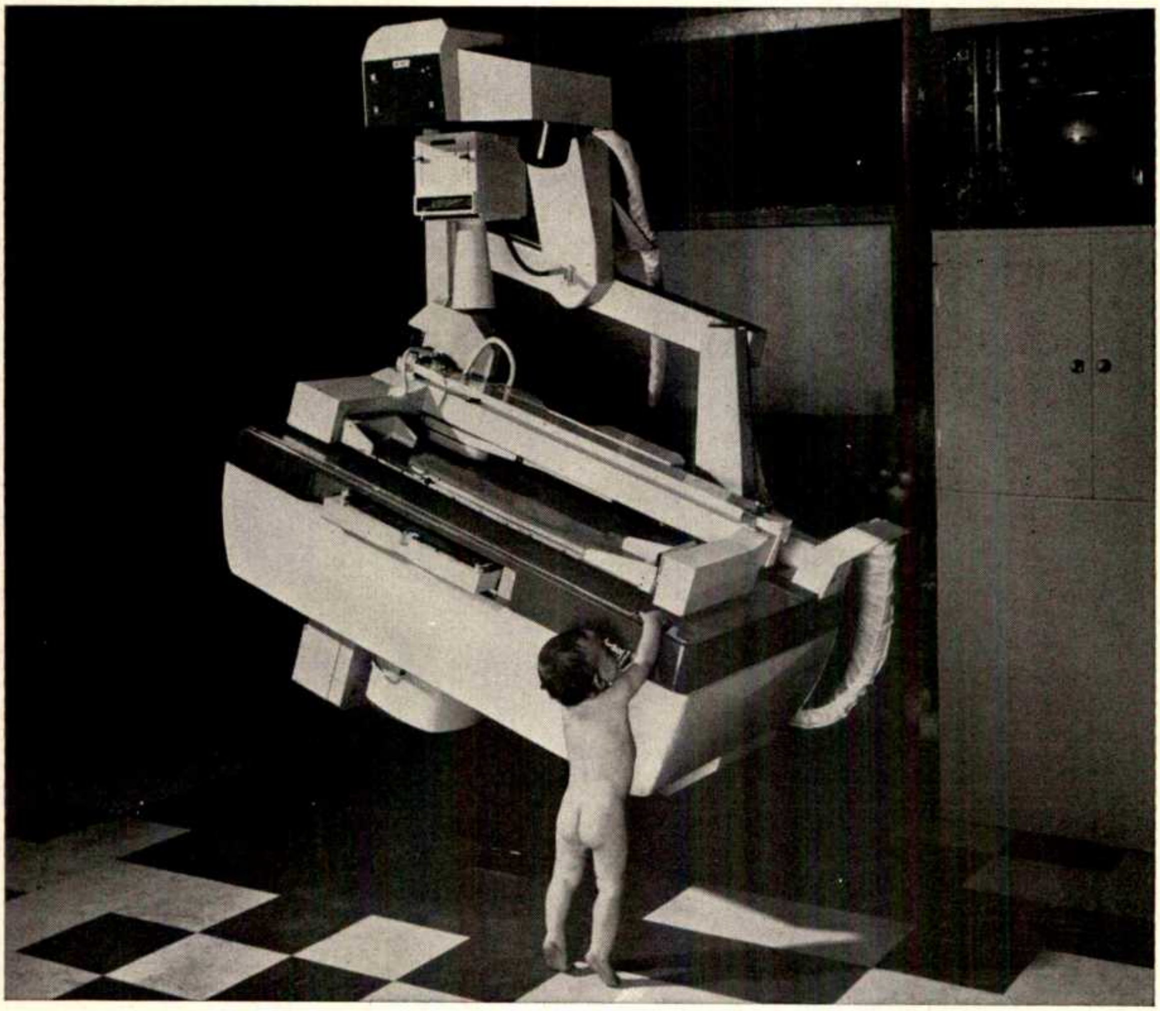
Didronel

etidronate disodium

Brocades Great Britain Ltd.

Brocades House, Pyrford Road, West Byfleet, Weybridge,
Surrey KT14 6RA. Telephone Byfleet 45536/42291

A table designed specifically for all infant radiological investigations



PEDIATRIX
from
CGR

Specifically designed for pediatric radiography, the Pediatrix has interchangeable table tops for correct support according to patient size. There is easy access to the patient and remote control of all movements.

For examinations including pulmonary, digestive, urological, orthopaedic and tomographical.

Full details and specifications from
CGR MEDICAL LIMITED
Astronaut House, Feltham, Middx. Tel: 01-890 8166
Branches at: *Bristol, Cambridge, Edinburgh, Glasgow, Manchester, Nottingham*

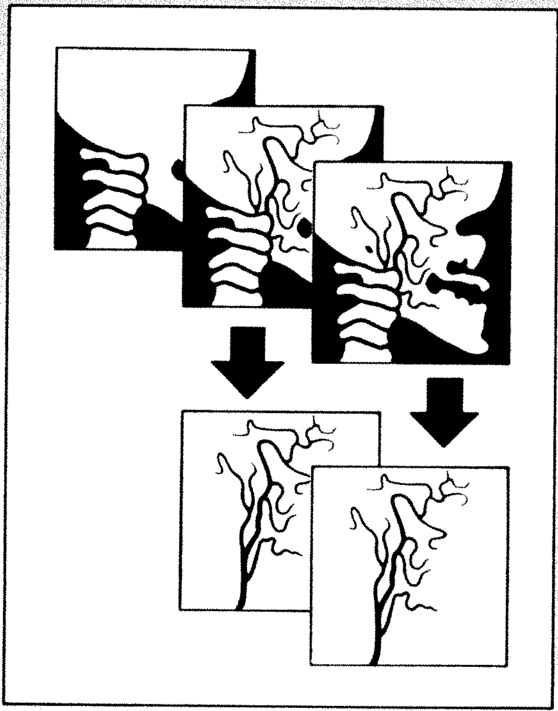
THAT MATTER.

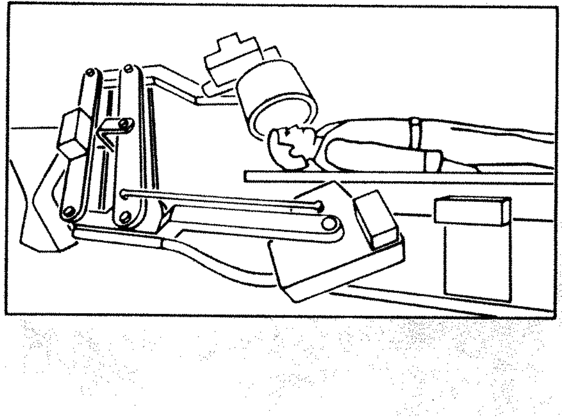
Digital vascular imaging.

DVI is an advanced digital processing system for performing intravenous angiography with real-time image subtraction.

DVI provides angiographic-calibre information achieved by IV contrast administration and is

- relatively non-invasive
- a low risk technique
- quick and simple
- easy to perform:
  - ○ no catheter manipulation
  - ○ no sterile technique
  - ○ no femoral puncture or cutdown
  - ○ no post-procedure patient monitoring
- an ideal outpatient procedure requiring no hospitalisation
- cost effective





DVI's clinical applications include:

- asymptomatic vascular disease screening
- evaluation of the high risk patient
- post-surgical evaluation and follow up
- an adjunct to both conventional and interventional angiography
- a "first order" diagnostic tool in lieu of conventional angiography

Because of DVI's unique subtraction and enhancement capabilities, other potential applications most certainly will develop with increased clinical usage.

PHILIPS

Medical Systems

For detailed information write to Philips Medical Systems, Kelvin House
63/75 Glenthorne Road, Hammersmith, London W6 0LJ.

THIS SITE
IS NOT
TO LET

It is a great many years since our first appearance, in alternate months, in this privileged position in the 'Journal'. Thinking about this led us to browse through our back files to some of our earliest regular appearances in print, with 'Cuthbert Andrews' advertisements:

1914 'Archives of the Roentgen Ray'
1915 'Journal of the Röntgen Society'
1916 'Archives of Radiology and Electrotherapy'
1923 'Journal of Scientific Instruments' (Issue No.1)
1924 'British Journal of Radiology' (the successor to 'Journal of the Röntgen Society')

with brief excursions into:

1918 'Recalled to Life' (Issue No.3)
1919 BEAMA Journal
1920 British Medical Journal
1920 'Nature'

While our founder, Mr. Cuthbert Andrews, was very active in the developing science (as 'C. H. F. Muller' from 1910 to 1914 and 'Cuthbert Andrews' thereafter) the doyen of the present staff can only claim personal experience from 1929 onwards. However, this substantial span does give us the edge over many others where X-ray accessories are concerned and allows us still to say...

Why not ask Andrews?

... and people keep on doing it – all over the world!

CUTHBERT ANDREWS
EVERYTHING X-RAY LTD.

5 HIGH STREET, BUSHEY VILLAGE, WATFORD WD2 1BE

Overseas telegrams:
EXRAYZE WATFORD

Telephone:
01-950 2525

Telex:
Evex 925859 Elwood G

1981, *British Journal of Radiology*, *54*, 1027–1033

VOLUME 54 NUMBER 648 DECEMBER 1981

The British Journal of Radiology

Enchondromata with annular calcification in association with fibrous dysplasia

By N. G. Sanerkin, M.D., F.R.C.P.E. and Iain Watt, M.R.C.P., F.R.C.R.

Departments of Osteoarticular Pathology and Radiology, Bristol Royal Infirmary and the Bristol Bone Tumour Registry

(*Received June 1981*)

ABSTRACT

Annular or ring calcification is described in conjunction with fibrous dysplasia in four of 110 patients culled from the Bristol Bone Tumour Registry. This feature results from endochondral calcification and ossification within cartilage rests or chondromata developing *pari passu* with fibrous dysplasia. Statistically the condition is more likely to be present in the polyostotic form of fibrous dysplasia (17%) than in the monostotic form (*circa* 1%).

All patients were male and the diagnosis of fibrous dysplasia was established between the time of birth and the age of 16. Ring calcification was first detected between the ages of three and 16 years and persisted into adult life. Calcification almost exclusively involved the lower limbs particularly around the knee and above the ankle. In the three polyostotic cases rapid and gross extension of the cartilaginous component of the disease occurred at the time of the adolescent growth spurt.

When present in a patient with fibrous dysplasia the appearances are typical and signify an associated benign enchondromatous process. No suspicion of chondrosarcoma should arise.

Islands of cartilage have been reported in about 10% of cases of fibrous dysplasia of bone, particularly of the polyostotic form (Harris *et al.*, 1962; Stewart *et al.*, 1962; Van Horn *et al.*, 1963) but its precise nature and significance have remained unclear. Various explanations have been offered for its presence, including callus formation following trauma (Harris *et al.*, 1962), metaplasia (Dahlin, 1967), dyschondroplasia or as a further manifestation of a connective tissue dysplasia (Stewart *et al.*, 1962; Van Horn *et al.*, 1963; Pelzmann *et al.*, 1980).

Classical radiological descriptions of fibrous dysplasia (Gibson and Middlemiss, 1970; Murray and Jacobson, 1977) have not emphasized the presence or significance of radiological calcification in fibrous dysplasia of bone, although one gross example has been reported (Pelzmann *et al.*, 1980).

The radiographic and pathological material of all patients with fibrous dysplasia of bone, classified by the Bristol Bone Tumour Registry, has been reviewed in order to elucidate the radiological and pathological features of this phenomenon.

MATERIAL

In the Bristol Bone Tumour Registry there were 110 cases of fibrous dysplasia, 18 polyostotic, 92 monostotic, and in all clinical radiographs and histological material were available for review. In one case, with very extensive cartilaginous involvement, an amputation specimen had been subjected to detailed examination.

RESULTS

Radiology

Four patients with cartilage formation were identified (3.6%), three with polyostotic fibrous dysplasia, one monostotic. In all there were extensive radiolucent zones associated with typical fibrous dysplasia. Within the radiolucent zones there was extensive annular or ring-like calcification (Fig. 1c). In some cases the lesions were confluent and in others more granular in appearance (Fig. 2A, B). All patients were male, the diagnosis of fibrous dysplasia being established at birth in one and by the age of 16 in the other three. Calcification was identified between the ages of three and 16. In all but one patient the calcification was confined to the lower limbs involving primarily the metaphysis and to a lesser extent the epiphysis and diaphysis. The principal clinical and radiological features are summarized below.

Case 1

A male infant presented at birth with gross skeletal deformity due to typical fibrous dysplasia involving the whole of the right side of the skeleton. During early childhood progressive femoral and tibial bowing required numerous

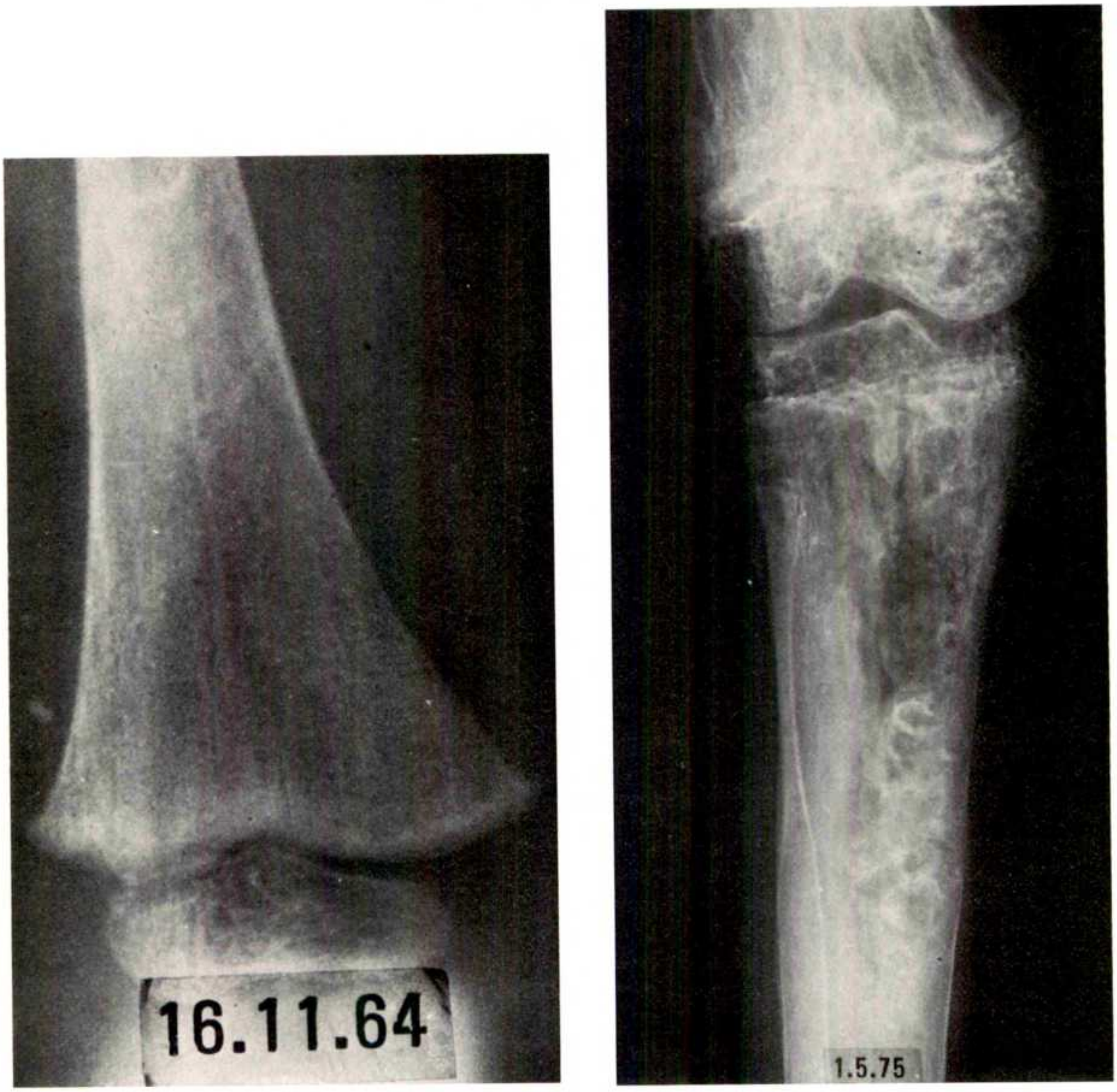


FIG. 1.

(A) Case 1 aged five years. The distal femoral diaphysis reveals only a slight alteration in trabecular pattern.

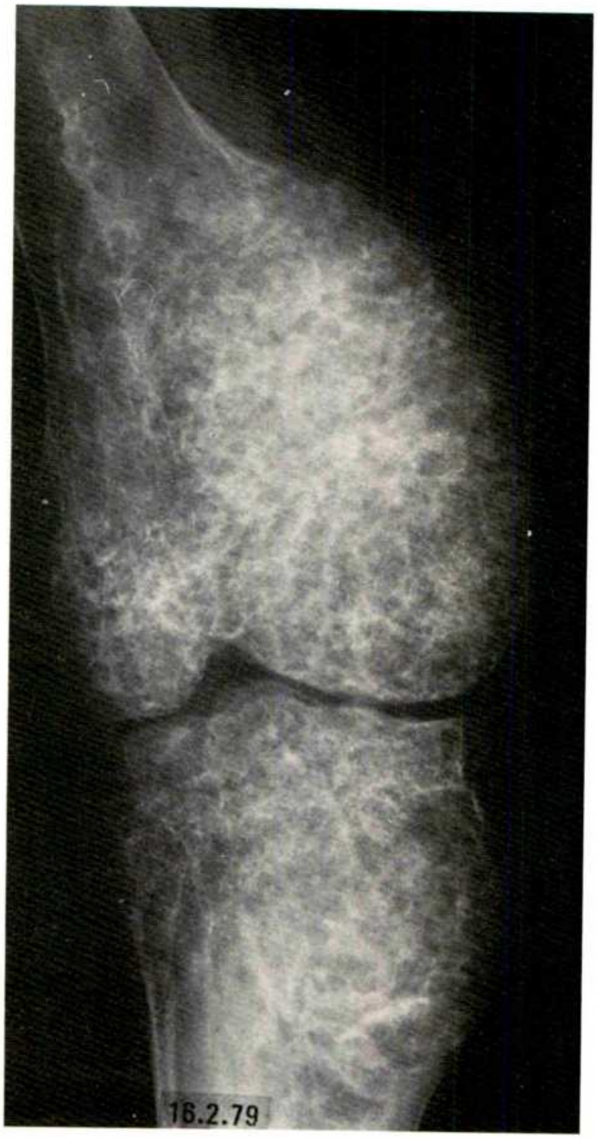
(B) Case 1 aged 12½ years. There are now gross changes of fibrous dysplasia. In addition there are radiolucent zones containing well marked annular or ring calcification. Both major epiphyses are involved.

osteotomies. He also sustained many fractures of the femur, tibia and humerus. However, severe bowing of the tibia recurred and eventually led to chronic offensive ulceration of the overlying skin and he had to be confined to a wheelchair. Between the ages of 13 and 14 there had been progressive enlargement of the distal femur and both ends of the tibia resulting in further disability. At age 17 a transfemoral amputation was performed for functional and aesthetic reasons.

Radiologically calcification had not been present at birth but became visualized in the right hip and distal femur at age five, and in the distal tibia at age seven (Fig. 3A–C). Lesions around the knee had become substantial by the age of 13 and gross by 17 (Fig. 1A–C).

Case 2

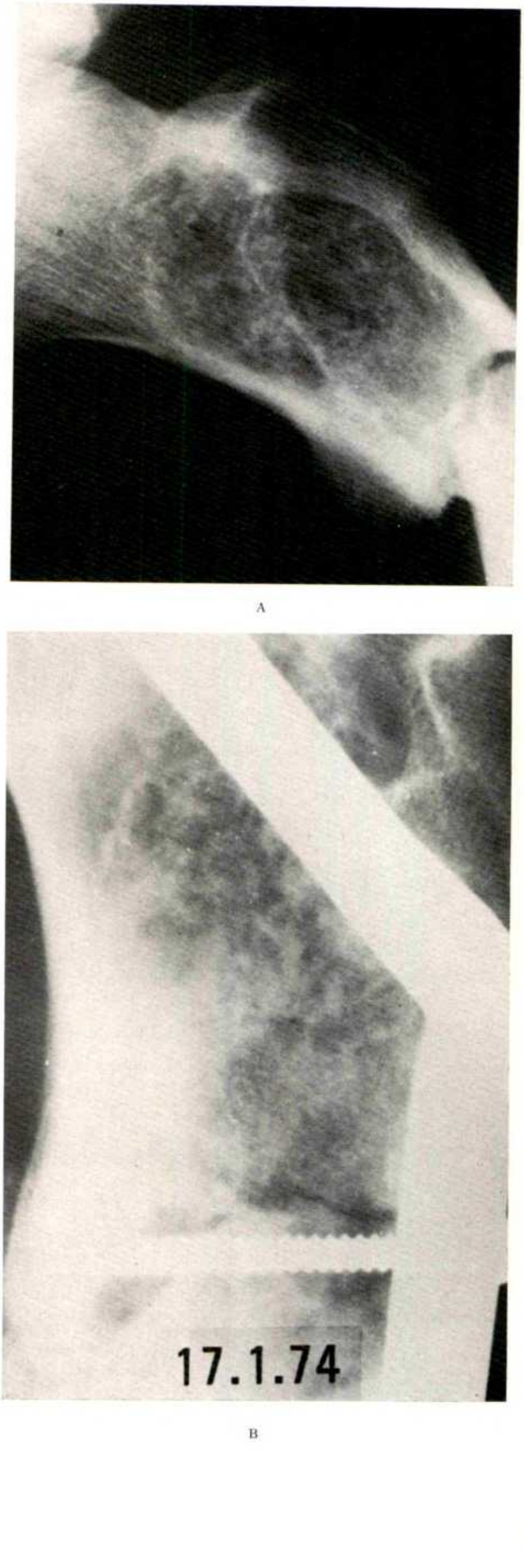
A two-year-old male presented with fibrous dysplasia involving both femora, tibae, fibulae and the right hemipelvis. Since early childhood he had suffered numerous fractures, developing bilateral coxa vara and tibial bowing, in the management of which he underwent numerous osteotomies with the insertion of intramedullary nails. Since the



C

FIG. 1.

(C) Case 1 aged 16¼ years. Gross extension of the cartilaginous components has occurred.

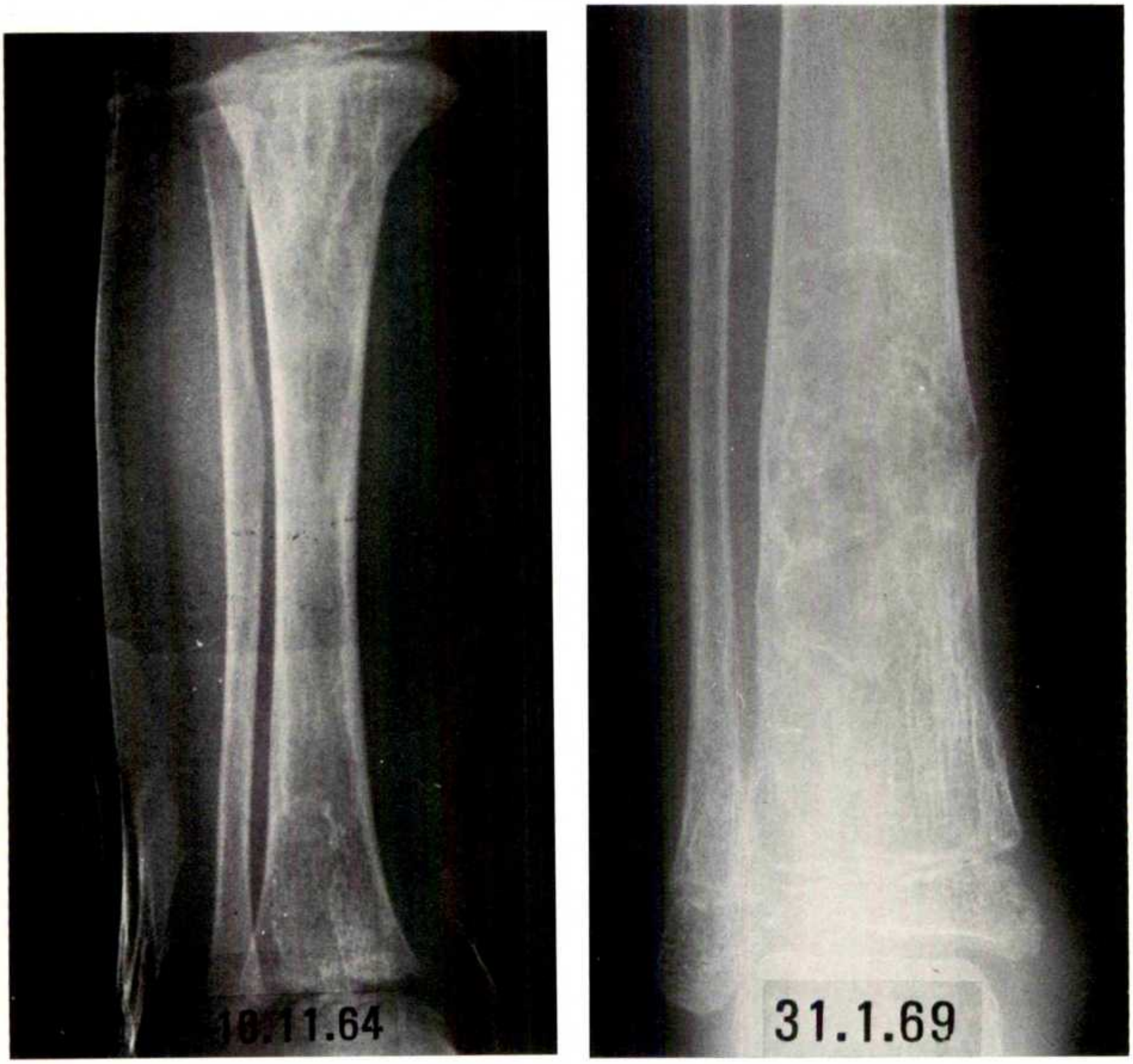


B

FIG. 2.

(A) Case 3 at presentation aged 16 years. There is a subtrochanteric pathological fracture through a radiolucent lesion, consistent with monostotic fibrous dysplasia. Within the translucency there is rather amorphous granular calcification.

(B) Case 3 after internal fixation. A localized view shows the annular component of the calcification.



A FIG. 3. B

(A) Case 1 aged two years. The whole tibia exhibits typical features of fibrous dysplasia.

(B) Case 1 aged 7¼ years. There are now well marginated translucent zones within the fibrous dysplasia. Possible annular calcification is present.

age of eight he had been on crutches. The patient was last seen at the age of 18 when an intramedullary nail was removed from the right tibia after it had perforated the skin.

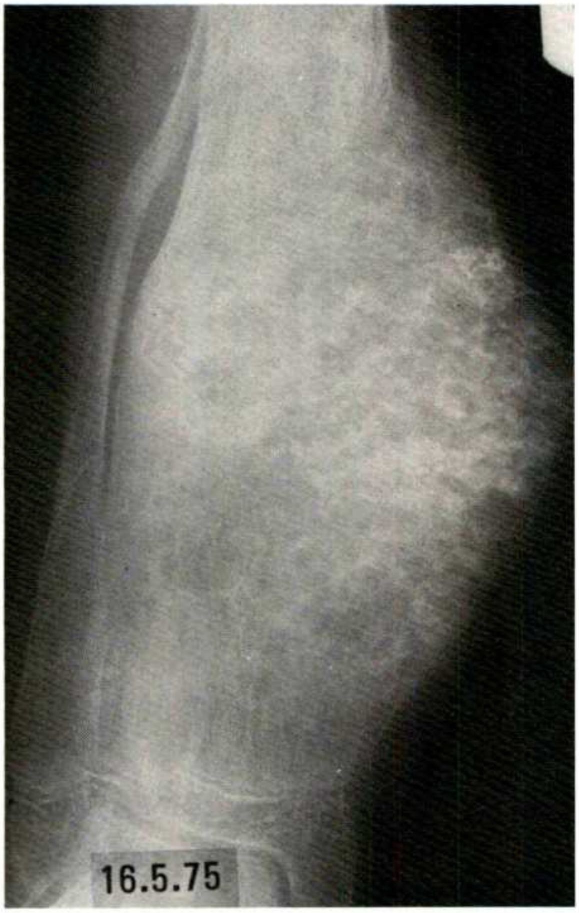
Radiographic calcification became visible first in the left distal femur at the age of three and progressed proximally during the following year. Calcification became marked by age seven and progressed considerably to the age of 18. Calcification was present in the right femur at the age of four extending proximally and distally, becoming gross between the ages of seven and 18. Calcification also developed in the left tibia which had been normal until the age of four and similarly became gross between the ages of eight and 18. Minor calcification was present in several metatarsals and in the right thumb metacarpal.

Case 3

A male aged 16 at presentation fell whilst playing football and sustained a pathological fracture of the left femur. Radiologically there were typical features of monostotic fibrous dysplasia within which there was granular and ring calcification (Fig. 2A). Internal fixation was achieved with a Jewitt nail plate. Union was delayed but was eventually sound (Fig. 2B).

Case 4

A male aged nine presented with skeletal deformity due to polyostotic fibrous dysplasia mainly involving the pelvis and right femur. Calcification in the femur was not present at initial examination (Fig. 4A) but was identified at the age



C

FIG. 3.

(C) Case 1 aged 13½ years. There is now gross eccentric expansion of the distal tibia with obvious annular and granular calcification.

of ten. Lesions became gross between the ages of 11 and 22 (Fig. 4B). The features were unchanged when last examined at the age of 32.

Pathology

Review of the pathological material from 110 patients revealed cartilaginous foci in eight cases (7%). In five (4.5%) the cartilage formed part of a fracture callus relating to an identifiable fracture

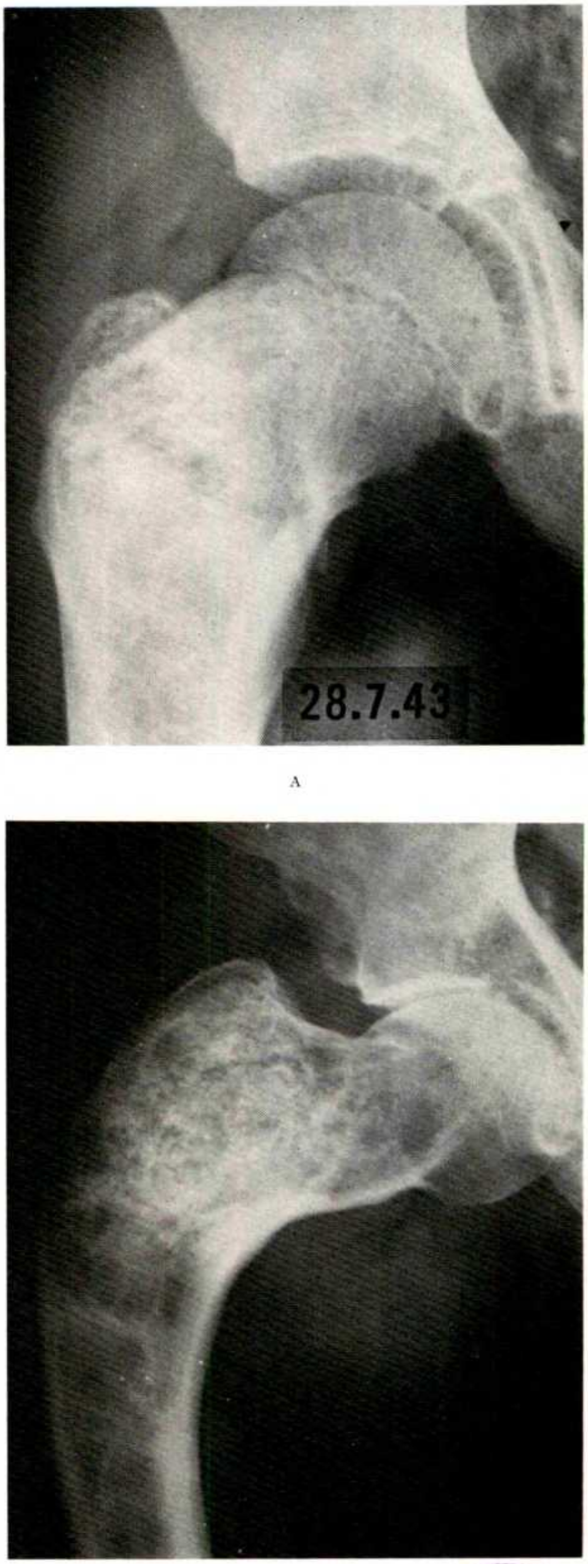
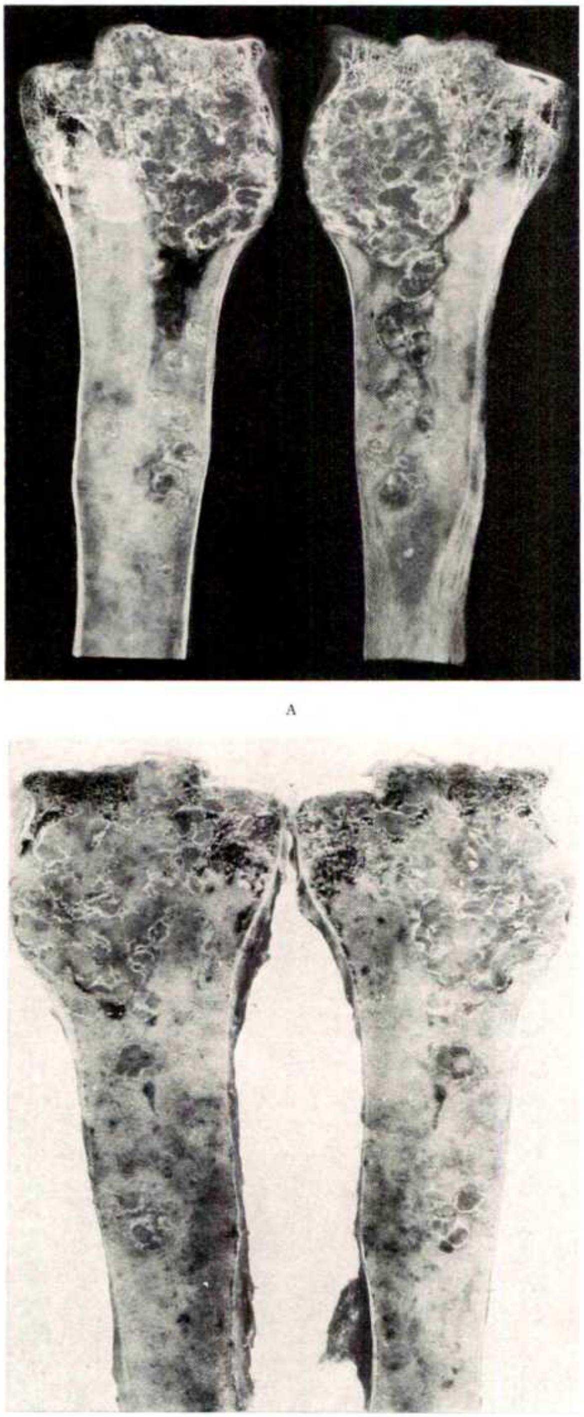


FIG. 4.

(A) Case 4 aged nine years. There is fibrous dysplasia of the proximal femur.

(B) Case 4 aged 32 years. There is acquired coxa vara with well marked annular and amorphous calcification in the intertrochanteric region.

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY
U. I.



A

B

FIG. 5.

Case 1 amputation (A) slab radiograph, (B) gross specimen. The tibia reveals the "ground glass" changes of fibrous dysplasia (grey uniform areas). The proximal tibia is replaced by conglomerate cartilaginous masses with annular calcification around individual nodules. Scattered cartilaginous lesions are present in the diaphysis.

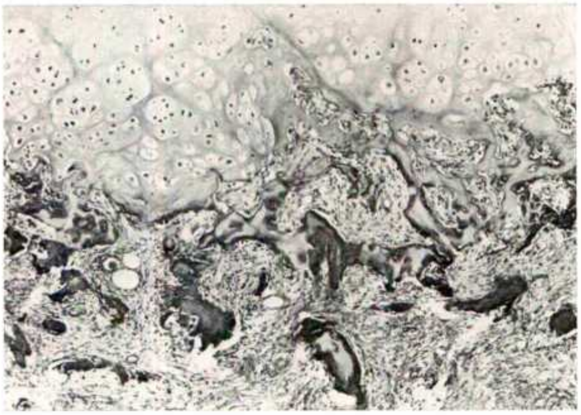


FIG. 6.

A rim of evolutionary ossification is shown surrounding a cartilaginous nodule. There are columns of necrotic calcified cartilage embedded in fibro-cellular tissue (haematoxylin and eosin × 50).

line and/or associated with reactive new bone formation in the cortex or sub-periosteal tissues. In no case had calcification under these circumstances been radiographically detected. In the remaining three patients, Cases 1, 2 and 3 above, there was extensive cartilage formation similar to that found in enchondromata or cartilage rests. In Case 4 material was available for review confirming the diagnosis of fibrous dysplasia but its site of origin was not from a cartilage-containing area. In three cases, therefore, where cartilaginous material could be studied, including the amputation specimen from Case 1, the chondromatous masses were intimately related to typical fibrous dysplasia of bone.

The histopathological findings were similar in all cases, and are best exemplified in the amputation specimen. Macroscopically very extensive fibrous dysplasia was found in all bones including the tarsus, metatarsus and phalanges. Islands of cartilage were present in all long bones and in some foot bones mainly in the metaphyses and epiphyses. The distal femur was grossly expanded and massively replaced by conglomerate cartilage masses. Chondromatous masses of only somewhat lesser proportions were found in the distal and proximal tibia (Fig. 5) and in the distal fibula.

Histologically, the fibro-osseous lesions showed the typical features of fibrous dysplasia—a fibrocellular proliferate, rich in alkaline phosphatase, with irregular ossicles of fibre bone. The chondromatous lesions showed relatively cellular, but nevertheless benign, cartilage of the type expected in skeletal enchondromatosis. The constituent cartilaginous nodules were rimmed by narrow zones of endochondral ossification, with calcified and partly ossified cartilage columns embedded in dysplastic fibro-osseous tissue (Fig. 6). Less often, when the cartilage abutted onto normal medullary tissue, there was a thin rim of mature lamellar bone.

DISCUSSION

Fibrous dysplasia is a developmental anomaly of ossification in which the osteoblasts fail to undergo normal morphological differentiation and maturation. They deviate partially along fibroblastic lines, undergoing fibrous metaplasia, but remain rich in alkaline phosphatase (Changus, 1957) and retain their osteogenic potential to some degree with production of fibre bone. Coexisting enchondromata or cartilage rests would be expected only in bones developing through endochondral ossification, as in the present series, the cartilaginous masses being an expression of enchondromatosis in association with fibrous dysplasia. None of the enchondromatous lesions was associated with reparative callus to indicate a traumatic aetiology and there were no features to suggest that the cartilaginous nodules arose through any chondroid metaplasia of dysplastic fibro-cellular tissue. The cartilaginous islands arise as developmental "rests" from epiphyseal cartilage and develop *pari passu* with the fibrous dysplasia. Lesions high in the diaphysis indubitably arose earlier in life and remained *in situ* as longitudinal growth progressed.

A similar association of "popcorn" calcification with cartilaginous nodules has been reported recently in patients with osteogenesis imperfecta (Goldman *et al.*, 1980). In that condition the lesions were predominantly metaphyseal and in the lower limbs but although they advanced, as in the present series, at the time of maximal skeletal growth they became radiologically no longer discernible at skeletal maturation, unlike those in fibrous dysplasia.

Radiologically all the lesions were similar. The well-marked annular or ring configuration seems characteristic. The rapid progression and extension of the cartilaginous lesions during the adolescent growth spurt may raise the erroneous suspicion of chondrosarcoma. Malignancy is a rare complication of fibrous dysplasia, with an overall incidence of about 0.4% (Schwartz and Alpert, 1964) and in the majority of cases this is an osteosarcoma or fibrosarcoma (Jaffe, 1958; Huvos *et al.*, 1972; Feintuch, 1973). From the published data it is not possible to speculate whether or not the few chondrosarcomas that complicated fibrous dysplasia were all related to pre-existing cartilaginous nodules. However, in two cases the relationship is unequivocal (Huvos *et al.*, 1972; Feintuch, 1973). In both cases published illustrations reveal an obvious area of purely osteolytic destruction arising in conjunction with an organized area of annular calcification suggesting malignant change in an antecedent benign cartilaginous lesion. In other cases a low grade chondrosarcoma may have been erroneously diagnosed (Pelzmann *et al.*, 1980). Provided the organized area of the ring calcification is uninterrupted or uncomplicated by an additional purely lytic, ill-defined zone, the possibility of chondrosarcoma can be discounted. The prognostic significance of the radiographic detection of calcification in fibrous dysplasia lies not, therefore, in the suggestion of potential malignancy but rather in the likelihood of subsequent further disfiguration, difficulties in orthopaedic management and cutaneous ulceration, particularly at the time of adolescent growth spurt.

ACKNOWLEDGMENTS

The authors are grateful to their clinical colleagues for their permission to report cases under their care.

REFERENCES

CHANGUS, G. W., 1957. Osteoblastic hyperplasia of bone: histochemical appraisal of fibrous dysplasia of bone. *Cancer*, *10*, 1157–1161.

DAHLIN, D. C., 1967. *Bone Tumors: General Aspect and Data on 3987 Cases*. 2nd edit. (C. C. Thomas, Springfield, Illinois), p. 238.

FEINTUCH, T. A., 1973. Chondrosarcoma arising in a cartilaginous area of previously irradiated fibrous dysplasia. *Cancer*, *31*, 877–881.

GIBSON, M. J. and MIDDLEMISS, J. H., 1970. Fibrous dysplasia of bone. *British Journal of Radiology*, *44*, 1–13.

GOLDMAN, A. B., DAVIDSON, D., PAVLOV, H. and BULLOUGH, P. G., 1980. "Popcorn" calcification: a prognostic sign in osteogenesis imperfecta. *Radiology*, *136*, 351–358.

HARRIS, W. H., DUDLEY, H. R. and BARRY, R. J., 1962. The natural history of fibrous dysplasia. An orthopaedic, pathological and roentgenographic study. *Journal of Bone and Joint Surgery*, *44A*, 207–233.

HUVOS, A. G., HIGINBOTHAM, N. L. and MILLER, T. R., 1972. Bone sarcomas arising in fibrous dysplasia. *Journal of Bone and Joint Surgery*, *54A*, 1047–1056.

JAFFE, H. L., 1958. *Tumors andTumorous Conditions of the Bones and Joints* (Lee & Febiger, Philadelphia), pp. 134–135.

MURRAY, R. O. and JACOBSON, H. G., 1977. *The Radiology of Skeletal Disorders*. 2nd edit. (Churchill Livingstone, Edinburgh/London/New York), pp. 890–897.

PELZMANN, K. S., NAGEL, D. Z. and SALYER, W. R., 1980. Case Report 114. *Skeletal Radiology*, *5*, 116–118.

STEWART, M. J., GILMER, W. S. and EDMONDSON, A. S., 1962. Fibrous dysplasia of bone. *Journal of Bone and Joint Surgery*, *44B*, 302–318.

SCHWARTZ, D. T. and ALPERT, M., 1964. The malignant transformation of fibrous dysplasia. *American Journal of Medical Sciences*, *241*, 35–54.

VAN HORN, P. E., DAHLIN, D. C. and BICKEL, W. H., 1963. Fibrous dysplasia; a clinical pathologic study of orthopedic surgical cases. *Proceedings of the Staff Meetings of the Mayo Clinic*, *38*, 175–189.

1981, *British Journal of Radiology*, *54*, 1034–1038

Lacrimal gland tumours: the role of CT and conventional radiology

By G. A. S. Lloyd, D.M., F.R.C.R.

Moorfields Eye Hospital, City Road, London EC1V 2PD

(*Received June 1981*)

Abstract

The X-ray features of 66 lacrimal gland tumours, comprising 32 benign pleomorphic adenomas, 24 carcinomas and ten lymphomas, are reviewed. The role of radiology in the management of these patients is discussed.

Although lacrimal gland tumours present no unique radiological appearances, the diagnosis and pathological type may be suggested by a combination of conventional radiography and CT scan. It is important to distinguish the pleomorphic adenoma clinically and radiologically from other lesions of the lacrimal gland, since this tumour must be excised *in toto*. Incisional biopsy or partial removal may result in a disastrous recurrence with seeding into bone and soft tissue. X-ray signs of malignancy in lacrimal gland tumours include invasion and sclerosis of the adjacent bone of the lacrimal fossa, calcification in the tumour and extension outside the lacrimal gland area shown on CT scan. The pre-operative diagnosis of malignancy was improved from 42% to 73% by CT.

Indentation or enlargement of the lacrimal fossa was seen in 80% of benign pleomorphic adenomas. Although non-specific, this sign in a patient with a painless lacrimal gland swelling of over 12 months' duration, without radiological evidence of malignancy, is strongly indicative of a benign tumour.

Since the report of Jones and Pfeiffer (1954), it has been recognized that lacrimal gland tumours may give rise to X-ray changes in the adjacent lacrimal fossa. These authors described bone changes in 18 of 20 patients with lacrimal gland tumours, recording bone erosion, invasion and sclerosis. Newton (1962), reviewed the X-ray features in 12 examples of epithelial lacrimal gland tumours including both benign mixed and malignant epithelial growths. More recently, Wright *et al.* (1979), in a comprehensive review of the management of 40 patients treated for lacrimal gland neoplasia, have emphasized the importance of radiology in the assessment of these patients and base their surgical approach on a combination of clinical and radiological findings. The introduction of CT for orbital diagnosis now allows the soft tissue mass of the lacrimal gland tumour to be shown in addition to bone changes. The purpose of this paper is to re-examine the role of radiology in the investigation of these patients and to assess the diagnostic criteria demonstrable both by CT and conventional X-ray techniques.

Case Material

Fifty-six patients with histologically proven epithelial tumours of the lacrimal gland have been investigated in the period 1967–1980. The age range was 14 to 77 years. Thirty-two patients were shown histologically to have a benign mixed tumour of the lacrimal gland. There were 22 carcinomas; these comprized 11 adenoid cystic carcinomas, six adenocarcinomas, five undifferentiated carcinomas and two

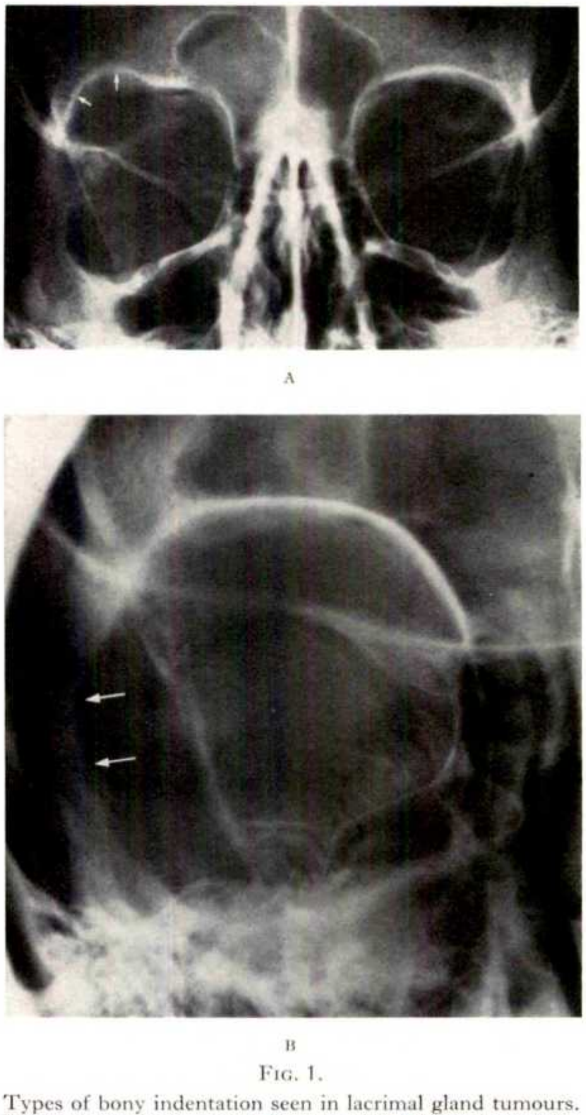


Fig. 1.

Types of bony indentation seen in lacrimal gland tumours. Enlargement may be upward or superolateral (A) or lateral (B).

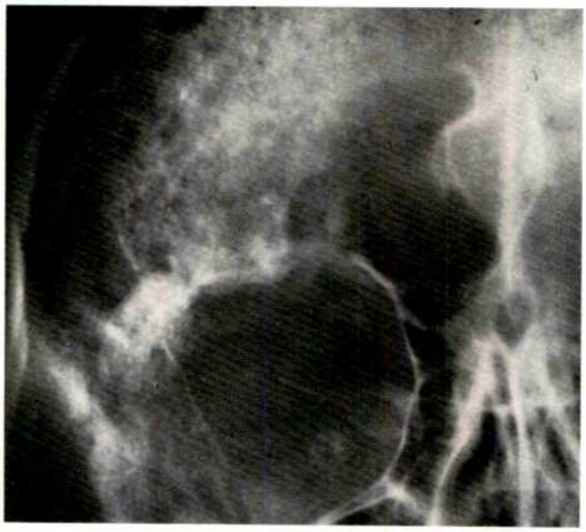


FIG. 2.
Extensive erosion of the frontal bone due to an adenocarcinoma of the lacrimal gland.

malignant epithelial tumours of ductal origin. In two further patients there was malignant change in a benign mixed tumour. In addition, during the same period, ten patients were shown to have a lymphoma of the lacrimal gland. In all a total of 66 patients were examined with histological proof of the type of tumour present.

RADIOLOGICAL FINDINGS

Indentation and enlargement of the lacrimal fossa

This is the result of a slowly expanding mass exerting pressure on the adjacent bone of the lacrimal fossa without direct invasion. There are two types of change discernible on plain X-ray: an overall enlargement of the lacrimal fossa with thinning and sometimes slight decalcification of the bone; or a more clear-cut indentation with a well-defined margin (Fig. 1A, B). Both changes are most often due to a benign pleomorphic tumour of the lacrimal gland, but the sign is non-specific since it was seen in 12 (50%) of the malignant tumours, and in four of these it was present in isolation without other changes indicative of malignancy. In the series as a whole, when present as an isolated phenomenon, pressure enlargement of the lacrimal fossa occurred in a benign/malignant ratio of 26:4. Coupled with a history of painless enlargement of the lacrimal gland of over 12 months' duration, it is strongly indicative of a benign mixed tumour (Wright *et al.*, 1979).

Bone destruction

This occurs either when a carcinoma of the lacrimal gland extends to invade the adjacent bone (Fig. 2), or when a mixed lacrimal gland tumour seeds into the frontal bone following incomplete surgical excision. In this series, direct bone invasion as opposed to pressure changes was always associated with malignancy. Early bone invasion may be shown on plain X-ray when fairly extensive, but is better demonstrated at an early stage either by hypocycloidal tomography or by high resolution CT (Fig. 3).

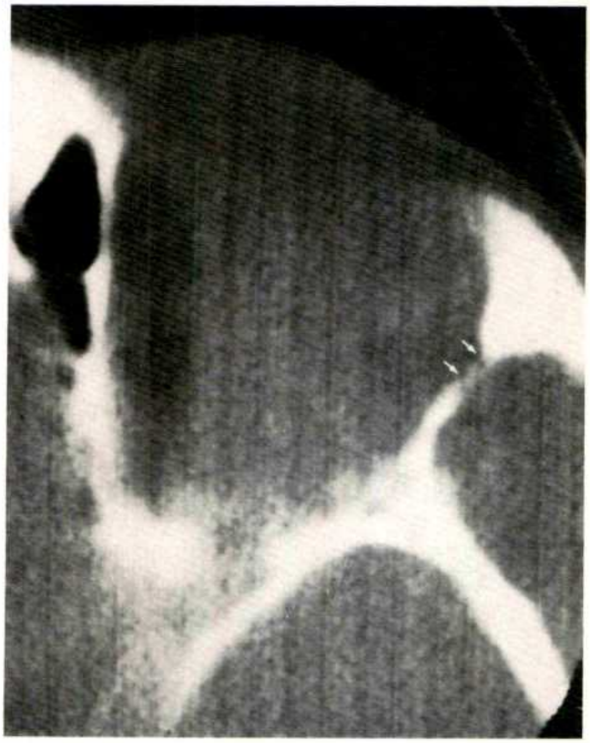


FIG. 3.
Early bone erosion shown on high resolution axial CT scan (arrows).

Increased density of the adjacent bone

Sclerosis in the adjacent bone of the lacrimal fossa was described by Newton (1962), and was considered to indicate a malignant tumour with a reactive type of bone invasion. In this series, two patients showed this change and both had malignant lacrimal gland tumours. In both instances the change was best shown on axial hypocycloidal tomography (Fig. 4).

Calcification

This was demonstrated in four patients by plain X-ray or by conventional tomography, and in three additional patients by CT, making a total of seven of the 56 epithelial tumours. Thus, using all techniques,

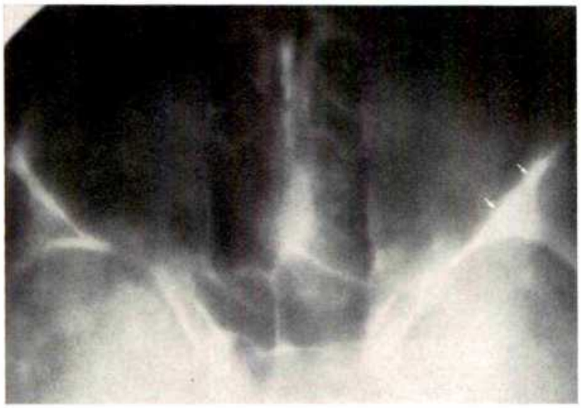
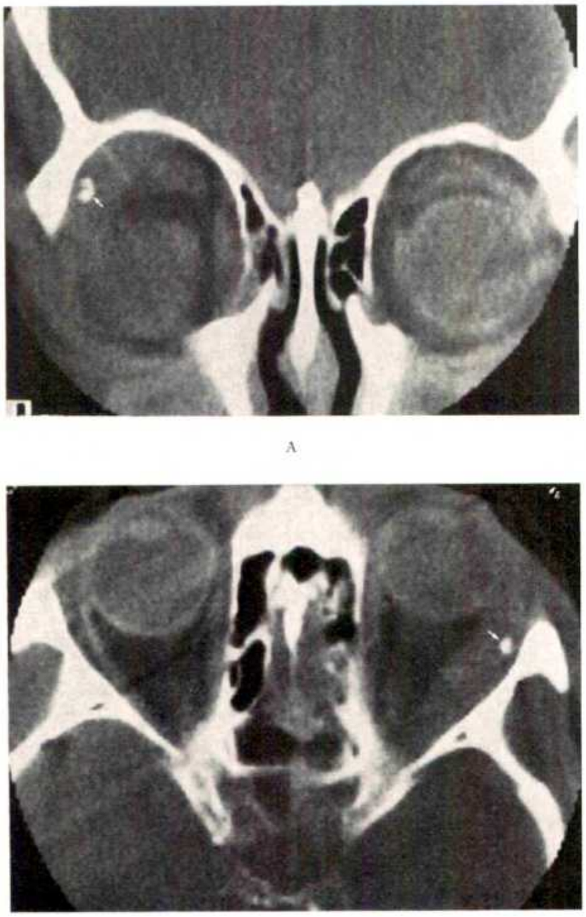


FIG. 4.

Carcinoma of the lacrimal gland. Bone sclerosis in the lateral wall of the orbit shown on axial hypocycloidal tomography (arrows).



A

B

FIG. 5.

Small nodule of calcification in an adenoid cystic carcinoma of the lacrimal gland shown on coronal (A) and axial (B) CT scan. The calcification was not diagnosed on plain X-ray.

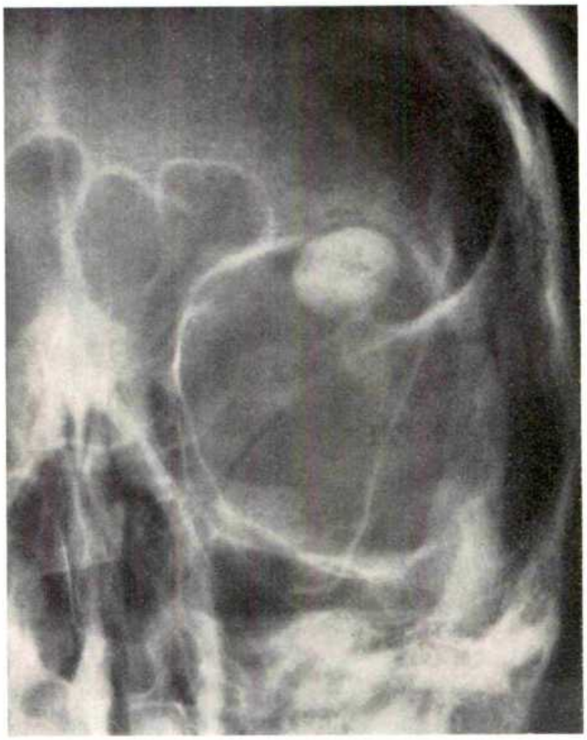


FIG. 6.

Large nodule of calcification in an adenoid-cystic carcinoma of the lacrimal gland.

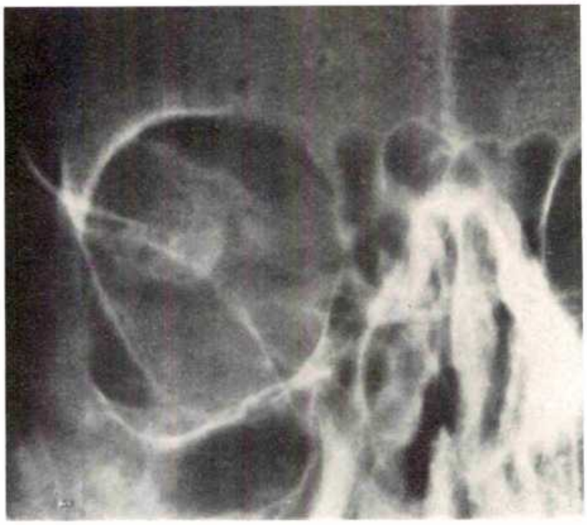
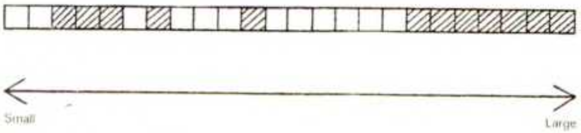


FIG. 7.

Diffuse calcification in a lacrimal gland carcinoma shown on plain X-ray.

TABLE I

24 LACRIMAL GLAND TUMOURS GRADED FOR RELATIVE SIZE AS SHOWN ON CT (12 BENIGN, 12 MALIGNANT)



☐	☐	▨	▨	▨	☐	▨	☐	☐	☐	▨	☐	☐	☐	☐	☐	☐	▨	▨	▨	▨	▨	▨	▨

Shaded squares malignant.
Blank squares benign.

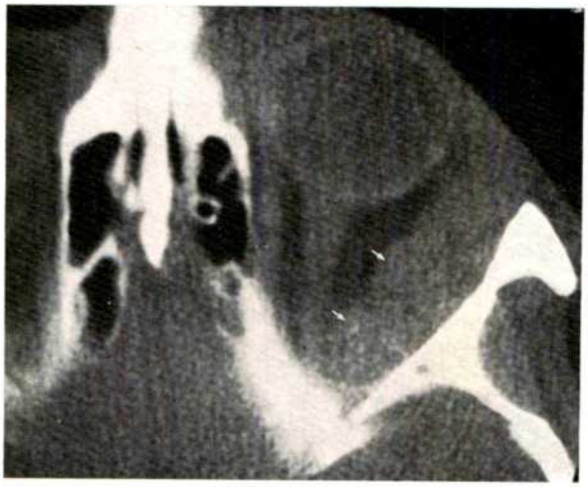


FIG. 8.

Axial CT scan. Extraconal extension of a carcinoma of the lacrimal gland to the orbital apex (arrows).

12.7% of patients showed calcification and in all patients the lacrimal gland tumour was shown histologically to be malignant. Calcification was either nodular, small (Fig. 5A, B), large (Fig. 6) or diffuse (Fig. 7).

CT scan

From the series of 56 patients, 34 were examined by CT; 18 of these had benign mixed tumours and 16 lacrimal gland carcinomas. Initially the patients were scanned using 160×160 matrix format, but later examinations have been carried out using an EMI CT 5005 Body Scanner incorporating a high resolution facility and routine two plane imaging (axial and coronal). CT scans in this series were reviewed in order to assess possible signs of malignancy, based upon the size, shape and extent of the lesion and the presence of calcification or bone destruction.

Table I shows the size distribution of the first 24 patients in the series who were examined by CT scan, the smallest to the left, the largest to the right. It will be seen that, as would be expected, the more extensive lesions were carcinomas; in fact the seven largest lesions in the series were all malignant. Nevertheless, there was a scatter of malignancies throughout the size range and there was no size below which it could be safely predicted that a given tumour would be benign. Irregularity of outline, and extension towards the orbital apex were also features of carcinomas (Fig. 8). However, in smaller carcinomas, while the capsule of the lacrimal gland remains intact, there is no way that they may be distinguished from a benign mixed tumour by their shape on CT scan.

Both pressure erosion and bone invasion may be demonstrated on CT scanning when a high-resolution system is used with wide window-width settings. Figure 3 shows bone invasion by a carcinoma of the lacrimal gland which was not shown by conventional techniques. In addition calcification in the lacrimal gland was demonstrated by CT in three patients when not demonstrated by plain X-ray. In all patients showing calcification the tumour was malignant.

DISCUSSION

The correct management of lacrimal fossa lesions depends upon recognizing the characteristic clinical and radiological presentation of benign mixed cell tumours so that biopsy in these patients is avoided and the capsule of the tumour remains intact at surgical excision (Wright *et al.*, 1979). If the capsule is breached or the tumour biopsied, tumour cells may seed into the surrounding tissues with disastrous consequences: the eventual outcome being similar to that of a carcinoma (Henk, 1981).

For malignant lacrimal gland tumours, a transeptal biopsy is required prior to treatment. In carcinomas, if there is no serious local spread or distant metastases, a radical resection may be attempted. Where there is inoperable local disease, treatment is by radiotherapy. It is therefore important to make some distinction between benign pleomorphic adenomas and malignant tumours of the lacrimal gland prior to surgical treatment. Clinically, the presence of pain is an important sign of possible malignancy, and the absence of pain, conversely, a strong indication of a benign lesion. Wright *et al.* (1979) based their clinical management of these patients on this sign coupled with length of history; a history of more than 12 months' duration usually indicates a benign lacrimal gland mass. The X-ray findings are clearly important to augment the clinical assessment of the patients. Signs of enlargement or indentation of the lacrimal fossa seen on plain

X-ray are reassuring, in the absence of radiological evidence suggesting malignancy (*e.g.* evidence of bone destruction, sclerosis or calcification in the tumour).

Neoplastic involvement of the lacrimal gland is not always due to epithelial tumours, but may be due to lymphoma. Ten patients were shown to have lymphomatous involvement of the lacrimal gland histologically in the period when this series of epithelial tumours was collected. A point of clinical differentiation is the age incidence; the average age of the lymphomas was 62.9 years, with an age range of 47–82 years. Epithelial tumours occur in a lower age group. In this series 30% of the malignant tumours and 22% of the benign tumours occurred in the second and third decades of life, the average ages being 43.7 years and 44.9 years respectively. Positive signs on plain X-ray in lymphomatous tumours of the lacrimal gland are usually minimal. Five patients (50%) showed minor local enlargement of the lacrimal fossa; the rest were negative to plain X-ray. CT scan was performed in five patients. In three the changes were confined to simple enlargement of the lacrimal gland, while in two the tumour was more widespread, showing as an extraconal mass, in one case infiltrating the rectus muscle cone.

CONCLUSIONS

1. The surgical necessity to excise the benign pleomorphic adenoma of the lacrimal gland *in toto* without an incisional biopsy, so that the danger of external seeding of the tumour is avoided, means that an attempt must be made by the radiologist to recognize the benign tumour of the lacrimal gland as opposed to the malignant epithelial tumour or lymphoma.

2. A combination of CT scanning and conventional X-ray techniques provided evidence of malignancy in 73% of lacrimal gland carcinomas. Signs suggesting malignancy were:
(a) invasion or sclerosis of adjacent bone;
(b) calcification in the tumour;
(c) the demonstration by CT of a large tumour mass spreading outside the lacrimal gland area or to the orbital apex.

3. The pre-operative diagnosis of malignancy in epithelial tumours of the lacrimal gland was improved from 42% to 73% by CT. In addition to showing the size and extent of the tumour in the orbit, CT also demonstrated calcification in the tumour when not revealed by plain X-ray or conventional tomography and in one patient, using high resolution CT, bone erosion was shown when not convincingly demonstrated by conventional tomography.

4. Eighty per cent of benign lacrimal tumours, and 50% of carcinomas, showed radiological enlargement or indentation of the lacrimal fossa. Although this sign is non-specific, when present in the absence of any positive radiological signs of malignancy in a patient complaining of a painless lacrimal gland swelling of over 12 months' duration, it strongly indicates a benign tumour.

REFERENCES

Henk, J. M., 1981. Orbital tumours. *Hospital Update*, *7*, 439–450.

Jones, I. S. and Pfeiffer, R. L., 1954. Lacrimal gland tumours: roentgenographic diagnosis. *Transactions of the American Academy of Ophthalmology*, *58*, 841–847.

Newton, T. H., 1962. Roentgen appearance of lacrimal gland tumours. *Radiology*, *79*, 598–605.

Wright, J. E., Stewart, W. B. and Krohel, G. B., 1979. Clinical presentation and management of lacrimal gland tumours. *British Journal of Ophthalmology*, *63*, 600–606.

Book review

Clinical Neuro-Ophthalmology. By B. Ashworth and I. Isherwood, 2nd edit, pp. 298, 1981 (Blackwell Scientific Publications), £32·50.
ISBN 0-632-00593-9

This book is a postgraduate text which presents those aspects of neurology important to the ophthalmologist. The second edition, now with an eminent co-author in Professor Isherwood, has been extensively revised. The book is intended primarily for the ophthalmologist, although offering guidance in diagnosis and management to both the trainee neurologist and radiologist. The chapter on radiology has also been revised since the original 1973 edition, to take account of the major import of computerized tomography in diagnosis and management. The work also covers retinal photography and electrical methods of investigation as well as traditional methods.

The book achieves its purpose admirably and in the reviewer's opinion is the ideal source of information on clinical neuro-ophthalmology for the radiologist requiring knowledge of the subject. It is a concise but comprehensive text, beautifully illustrated and with an extensive bibliography, and should be an important item on the bookshelf of every department of neuro-radiology. A single criticism concerns the amount of radiology included. One chapter of 60 pages in a book of 298 does not adequately reflect the importance of radiology, in an era when computerized tomography dominates the investigation in so many patients with neuro-ophthalmological disorders. An expansion of Professor Isherwood's excellent section would be welcome in future editions.

G. A. S. Lloyd.

1981, *British Journal of Radiology*, *54*, 1039–1043

DECEMBER 1981

Computed tomography in the localization of aldosterone-secreting adrenal adenomas

By D. R. Meek, M.B., Ch.B., J. G. Duncan, M.B., F.R.C.S., F.R.C.R.

Department of Radiology, The Royal Infirmary, Glasgow G4 0SF

and D. McAreavey, B.Sc., M.B., M.R.C.P.

Medical Research Council, Blood Pressure Unit, The Western Infirmary, Glasgow G11 6NT

(*Received January 1981 and in revised form May 1981*)

ABSTRACT

Computed tomography (CT) has been shown to detect both adrenal glands in 88.5% of upper abdominal examinations and can visualize at least one gland in 96.5% of patients. However, in examinations carried out specifically to visualize the adrenals, the glands were located in 98% of cases.

This technique was used in 18 patients with primary aldosteronism to localize aldosterone-secreting adrenal tumours and to distinguish these from non-adenomas (bilateral adrenal hyperplasia). The results were compared with quadric analysis, a statistical technique used to predict the likely surgical outcome.

In seven patients the CT results were verified by operation (six adenomas, one adrenal hypertrophy). However, in one further patient a large adenoma (20 mm in diameter) which had not been predicted by CT scanning was found at operation.

In the remaining ten patients who have been medically treated, results concordant with quadric analysis were obtained in eight cases.

We would suggest that CT scanning should be the initial investigation for the pre-operative localization of adenomas but further comparative studies are required.

Primary aldosteronism is usually caused by an aldosterone-secreting adrenal adenoma (Conn's syndrome); less commonly it may be the result of bilateral adrenal hyperplasia. It is important to differentiate these two causes because the treatment of choice is different; surgical excision for unilateral adenoma and long term therapy with potassium-sparing diuretics for bilateral hyperplasia (Ferriss *et al.*, 1975).

Pre-operative localization of adrenal tumours is of clinical importance because these tumours are often small and when centrally situated in the adrenal gland may be difficult or impossible to find at operation. The techniques used for this purpose include adrenal venography and adrenal vein plasma aldosterone measurements (Bucht *et al.*, 1964; Starer, 1965), adrenal arteriography (Kahn, 1967) and radionuclide imaging (Conn *et al.*, 1972), each with its limitations. We report our experience in the pre-operative localization of adrenal adenomas using the more recently introduced technique of computed tomography (CT).

PATIENTS AND METHODS

Patients

Eighteen patients were studied, each with high blood pressure (mean 189/114±24/12 mmHg) and biochemical evidence of primary aldosteronism (low serum potassium 2.9±0.5 mmol/l, low plasma active renin 7.2±5.5 μU/ml, and high plasma aldosterone 29.5±12.3 ng/dl).

Quadric analysis

This statistical technique was devised to distinguish adrenal adenomas from bilateral adrenal hyperplasia pre-operatively, using age, blood pressure and biochemical findings in peripheral blood. Having developed the technique, Aitchison *et al.* (1971) were able to predict the operation result correctly in eight cases. Subsequent prospective use of the technique allowed adenoma or hyperplasia to be correctly predicted in 23 out of 24 patients (Ferriss *et al.*, 1978). Its use in this series was to provide a diagnosis with which CT findings could be compared particularly in the unoperated group.

CT scanning

An EMI 5005/23 whole body scanner having a reconstruction matrix of 320×320 was used. The earlier scans were carried out using a 13 mm collimated beam with a field size of 320 mm and the later scans a 7 mm collimated beam and a 240 mm field size. The larger field size has a pixel size of 1 mm and the pixel size of the smaller field size is 0.75 mm. For high contrast difference (>10%) the smallest detail that can be discriminated is 1.5 times the pixel size (Philips, 1978). This suggests that lesions as small as 1.1 mm should be visualized with the smaller field size provided a sufficient density difference is present.

The patients were given dilute Gastrografin orally to outline the adjacent small bowel and hyoscine-*n*-butyl bromide (Buscopan) to act as an antiperistaltic agent. The patients were scanned from the diaphragm to the renal hilum so that the whole area occupied by the adrenal glands was visualized. The individual scans were carried out at 7 mm shifts to give adjacent or slightly overlapping slices. Intravenous contrast enhancement was not used.

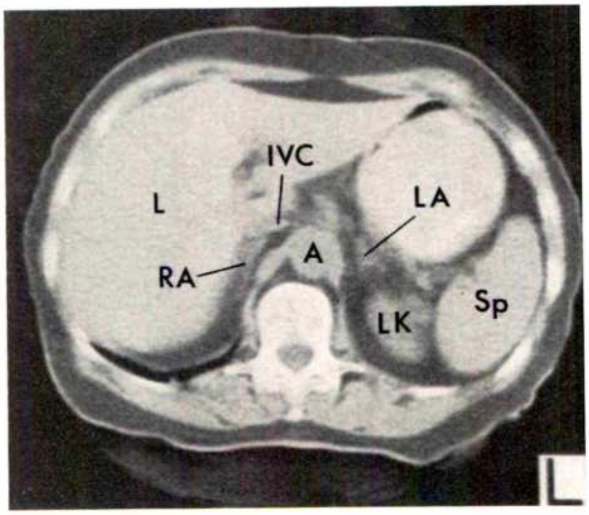


Fig. 1.
Normal adrenal glands. RA, Right adrenal; LA, Left adrenal; A, Aorta; IVC, Inferior vena cava; L, Liver; Sp, Spleen; LK, Left Kidney.

Normal adrenal glands (Fig. 1) may vary in shape and position (Brownlie and Kreel, 1978; Montagne *et al.*, 1978). The ability of the CT scanner to detect adrenal glands was studied in 200 patients who were examined for other reasons without clinical suspicion of any adrenal disease, using the 320 mm field size and 15 or 20 mm intervals between slices. A further 50 cases with a variety of adrenal diseases, excluding primary aldosteronism, were examined using the smaller field size as described above.

An adrenal adenoma when present usually deforms the gland outline (Figs. 2 and 3).

Results

Visualization of adrenal glands

In the retrospective review of 200 randomly selected patients in whom CT scans were carried out to demonstrate hepatic or renal lesions it was possible to visualize both adrenal glands in 177 cases (88.5%), despite a large slice interval. The right adrenal gland was seen in a further eight instances and the left in eight of the remainder.

In the second series of 50 cases the left adrenal gland was seen in 48 cases. The right adrenal gland was clearly visualized in 43 cases and in a further five instances a mass was seen replacing the right adrenal gland. Two glands (one left, one right) had previously been removed. Therefore in this series only two adrenal glands (one right, one left) which were presumed to be present were not seen (2%).

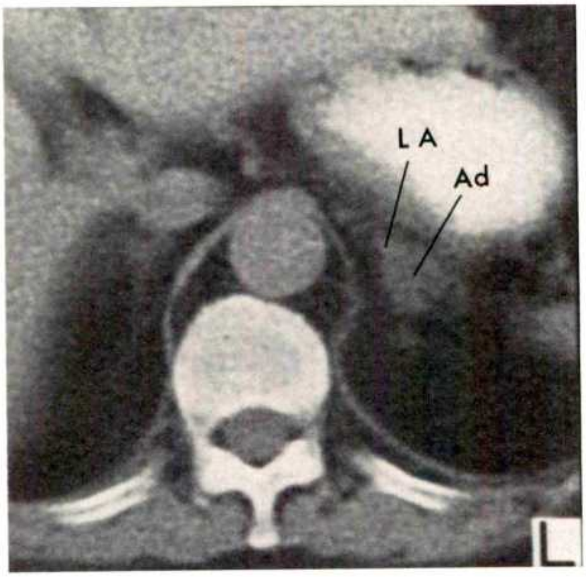


Fig. 2.
Adenoma of left adrenal gland. LA, Left adrenal; Ad, Adenoma.

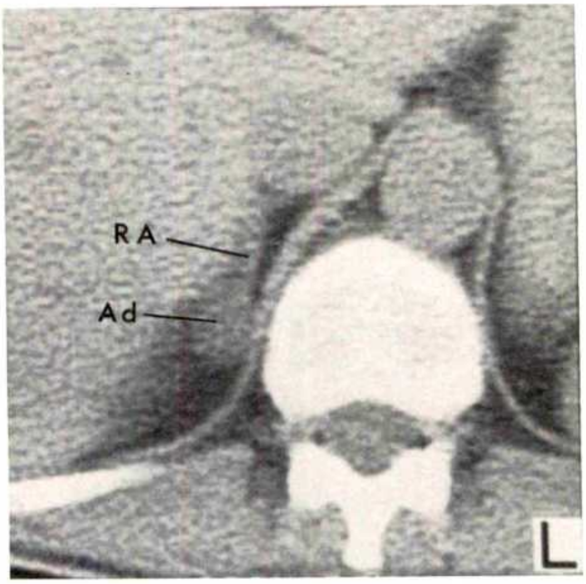


Fig. 3.
Adenoma of right adrenal gland. RA, Right adrenal; Ad, Adenoma

TABLE I

OPERATED CASES

Quadric analysis (odds in favour of diagnosis)		CT diagnosis (diameter of adenoma)	Operation (diameter of adenoma)
Adenoma	10:1	L. adenoma (6 mm)	L. adenoma (4 mm)
Adenoma	11:1	L. adenoma (11 mm)	L. adenoma (22 mm)
Adenoma	90:1	L. adenoma (12 mm)	L. adenoma (7.5 mm)
Adenoma	112:1	L. adenoma (15 mm)	L. adenoma (10 mm)
Adenoma	11:1	R. adenoma (13 mm)	R. adenoma (15 mm)
Non-adenoma	4:1	R. adenoma (17 mm)	R. adenoma (12 mm)
Adenoma	36:1	L. adrenal hyperplasia	L. adrenal hyperplasia
Adenoma	2:1	Normal glands	L. adenoma (20 mm)

TABLE II

UNOPERATED CASES

Quadric analysis (odds in favour of diagnosis)		CT diagnosis (diameter of adenomas)	
Adenoma	6:1	L. adenoma	(22 mm)
Adenoma	2:1	L. adenoma	(28 mm)
Adenoma	2:1	L. adenoma	(10 mm)
Adenoma	32:1	L. adenoma	(20 mm)
Adenoma	15:1	L. adenoma	(14 mm)
Adenoma	144:1	L &R adenomas	(L 15 mm) (R 18 mm)
Non-adenoma	94:1	Normal glands	
Non-adenoma	8:1	Normal glands	
Non-adenoma	4:1	R. adenoma	(15 mm)
Non-adenoma	7:1	R. adenoma	(10 mm)

Primary aldosteronism

In the 18 cases with biochemical evidence of primary aldosteronism the right adrenal gland was visualized in all cases and the left in 17 cases. Eight cases have subsequently had unilateral adrenalectomy (Table I) and in seven of these operation confirmed the CT findings (six adenomas, one adrenal hyperplasia). In the remaining patient the CT scan was normal, yet operation revealed a 20 mm diameter adenoma situated within the gland. In this case post-operative review of the scan and print-out still failed to demonstrate an adenoma.

Ten patients with primary aldosteronism have been medically treated (Table II). The reasons for elective long-term medical management include patients' reluctance to undergo surgery (three), advanced renal failure (one), persistent neutropenia (one), probable bilateral adrenal hyperplasia (one), dexamethasone suppressible hyperaldosteronism (one), bilateral adenomas (one), and age (two). In each of these cases the CT findings were compared with the diagnosis suggested by quadric analysis, which has proved reliable both in previous larger series (Aitchison *et al.*, 1971; Ferriss *et al.*, 1978) and in the operated cases in this study (Table I). Concordant results were obtained in eight cases with discrepancies in two, in each of which adenomas as detected by CT were not suggested by quadric analysis.

DISCUSSION

There are limitations to the conventional methods of visualization of the adrenal glands. An adrenal lesion smaller than 5 cm is rarely detected using intravenous urography and tomography either by direct visualization or by deviation of the kidney (Sutton, 1975). Ultrasonography only outlines the adrenal gland when it is considerably enlarged (Davidson *et al.*, 1975) although with newer techniques this may become a more sensitive tool (Sample, 1977). Radionuclide imaging is non-invasive and has been used successfully to locate aldosterone-secreting adenomas as small as 8 mm in diameter (Conn *et al.*, 1972). It has disadvantages in that the examination may take two to three weeks to complete and spatial resolution can be poor because of radioactive dose limitations (Hogan *et al.*, 1976; Kirschner *et al.*, 1975). Bilateral adrenal vein catheterization to allow both adrenal venography and adrenal vein plasma aldosterone assay gives good results but the technique is invasive and can be technically difficult (Reuter *et al.*, 1967; Mitty *et al.*, 1973); serious complications have been reported (Bayliss *et al.*, 1970; Fisher *et al.*, 1971). The detailed results obtained at bilateral adrenal vein catheterization in a larger series of patients will be reported elsewhere.

Published accounts of CT scanning in the localization of adrenal adenomas in primary aldosteronism are limited and show varying success (Karstaedt *et al.*, 1978; Dunnick *et al.*, 1979; Linde *et al.*, 1979). The reported adenomas have exceeded 10 mm in diameter, with a single exception which measured "less than 1 cm" (Karstaedt *et al.*, 1978). The smallest adenoma seen in our series was 6 mm in diameter and the largest 22 mm, with a mean of 13.5 mm.

One large adenoma measuring 20 mm in diameter was detected by adrenal venography and adrenal vein plasma aldosterone assay but not by CT. There are a few possible reasons for non-visualization of adenomas. Firstly, as reported by Montagne *et al.* (1978) difficulty in visualization of adenomas may occur when there is a lack of retroperitoneal fat. This causes the organs to be in close apposition and adenomas may be misinterpreted as parts of adjacent organs, *e.g.*, partial volume of the upper pole of the kidney or a loop of bowel which has not been opacified with Gastrografin.

Secondly, in CT scanners there is a compromise between low noise and spatial resolution. Although when a high density difference ($>10\%$) is present it is possible to detect structures as small as 1.5 times the pixel size, at low density differences (1%) structures may require to be three to four times the pixel size (2.2–3 mm with the 240 mm field size) to be visualized (Philips, 1978). Adenomas of the adrenals can have low densities (Schaner *et al.*, 1978). It is possible that the density difference between the adenoma and the surrounding fat is less than 1% and it cannot therefore be differentiated. These problems are increased if the scans are degraded by movement artefacts, *e.g.* due to bowel peristalsis.

Review of the scans of the patient in whom the adenoma was missed showed that there was a lack of retroperitoneal fat, and we feel that the reason for "non-visualization" of the adenoma was one of misinterpretation.

Another potential difficulty, although not encountered in this series, and not reported elsewhere, is that a large hyperplastic nodule may be misdiagnosed as an adenoma.

Previous evidence suggests that in adrenal hyperplasia the glands may be normal in size or only slightly enlarged (Karstaedt *et al.*, 1978; Korobkin *et al.*, 1979). In this series one case of hyperplasia of the left adrenal was diagnosed by computed tomography and subsequently confirmed histologically (Fig. 4).

In seven of our eight operated cases CT correctly located the lesion (87.5% accuracy) with no false positive indication of tumour. This compares favourably with the more invasive techniques—adrenal venography and adrenal vein plasma aldosterone assay (Clarke *et al.*, 1979; Horton and Finck, 1972).

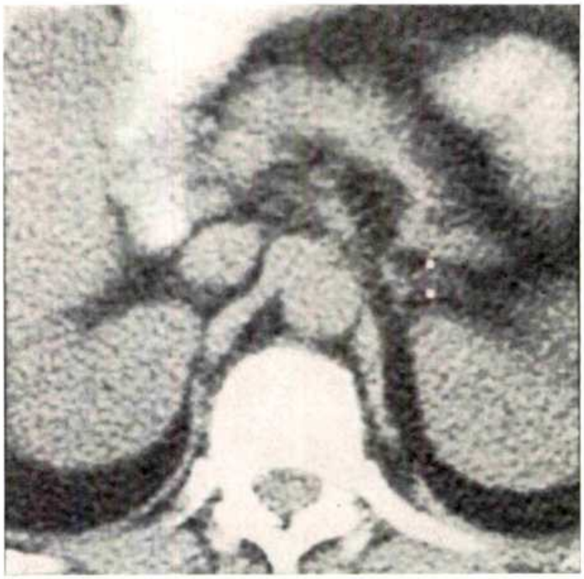


FIG. 4.

Hyperplasia of left adrenal showing electronic markers on the enlarged lateral limb of the gland. Length between markers: 0.8 cm.

In the unoperated series, the pathological diagnosis necessarily remained in doubt. Quadric analysis gave concordant results in eight of the ten cases (80% accuracy). In five of these eight cases the results of adrenal vein plasma aldosterone assay and adrenal venography were also in agreement.

These results support the view that CT scanning is a reliable technique for locating small adrenal adenomas (Karstaedt *et al.*, 1978). We would suggest that it should be the initial investigation for preoperative detection, although experience is limited and further comparative studies are required.

REFERENCES

AITCHISON, J., BROWN, J. J., FERRISS, J. B., FRASER, R., KAY, A. W., LEVER, A. F., NEVILLE, A. M., SYMINGTON, T. and ROBERTSON, J. I. S., 1971. Quadric analysis in the pre-operative distinction between patients with and without adreno-cortical tumours in hypertension with aldosterone excess and low plasma renin. *American Heart Journal*, *82*, 660–671.

BAYLISS, R. I. S., EDWARDS, O. M. and STARER, F., 1970. Complications of adrenal venography. *British Journal of Radiology*, *43*, 531–533.

BROWNLIE, K. and KREEL, L., 1978. Computer assisted tomography of normal suprarenal glands. *Journal of Computer Assisted Tomography*, *2*, 1–10.

BUCHT, H., BERGSTRÖM, J., LINDHOLMER, B., WIJNBLADH, H. J. and HÖKFELT, B., 1964. Catheterization of the left adrenal vein for contrast injection and steroid analysis in a case of Conn's syndrome. *Acta Medica Scandinavica*, *176*, 233–241.

CLARKE, D., JOHNSTON, I. D. A., WILKINSON, R., HACKING, P. M. and HACKITH, J. W., 1979. Severe hypertension in primary aldosteronism and good response to surgery. *Lancet*, *i*, 482.

CONN, J. W., MORITA, R., COHEN, E. L., BEIERWALTES, W. H., MCDONALD, W. J. and HERWIG, K. R., 1972. Primary aldosteronism. Photoscanning of tumours after administration of ^{131}I-19-iodocholesterol. *Archives of Internal Medicine, 129*, 417–425.

DAVIDSON, J. K., MORLEY, P., HURLEY, G. D. and HOLFORD, N. G., 1975. Adrenal venography and ultrasound in the investigation of the adrenal gland: an analysis of 58 cases. *British Journal of Radiology, 48*, 435–450.

DUNNICK, N. R., SCHANER, E. G., DOPPMAN, J. L., STROTT, C. A., GILL, J. R. and JAVADPOUR, N., 1979. Computer tomography in adrenal tumours. *American Journal of Roentgenology, 132*, 43–46.

FERRISS, J. B., BEEVERS, D. G., BROWN, J. J., FRASER, R., LEVER, A. F., PADFIELD, P. L. and ROBERTSON, J. I. S., 1978. Low-renin ("primary") hyperaldosteronism. *American Heart Journal, 95*, 641–658.

FERRISS, J. B., BROWN, J. J., FRASER, R., HAYWOOD, E., DAVIES, D. L., KAY, A. W., LEVER, A. F., ROBERTSON, J. I. S., OWEN, K. and PEART, W. S., 1975. Results of adrenal surgery in patients with hypertension, aldosterone excess and low plasma renin concentration. *British Medical Journal, i*, 135–138.

FISHER, C. E., TURNER, F. A. and HORTON, R., 1971. Remission of primary hyperaldosteronism after adrenal venography. *New England Journal of Medicine, 285*, 334–336.

HOGAN, M. J., MCRAE, J., SCHAMBELAN, M. and BIGLIERI, E. G., 1976. Location of aldosterone-producing adenomas with ^{131}I-19-iodocholesterol. *New England Journal of Medicine, 294*, 410–414.

HORTON, R. and FINCK, E., 1972. Diagnosis and localisation in primary aldosteronism. *Annals of Internal Medicine, 76*, 885–890.

KAHN, P. C., 1967. Selective angiography of the inferior phrenic arteries. *Radiology, 88*, 1–8.

KARSTAEDT, N., SAGEL, S. S., STANLEY, R. J., MELSON, G. L. and LEVITT, R. G., 1978. Computed tomography of the adrenal gland. *Radiology, 129*, 723–730.

KIRSCHNER, A. S., ICE, R. D. and BEIERWALTES, W. H., 1975. Radiation dosimetry of ^{131}I-19-iodocholesterol. The authors reply. *Journal of Nuclear Medicine, 16*, 248–249.

KOROBKIN, M., WHITE, E. A., KRESSEL, H. Y., MOSS, A. A. and MONTAGNE, J-P., 1979. Computed tomography in the diagnosis of adrenal disease. *American Journal of Roentgenology, 132*, 231–238.

LINDE, R., COULAM, C., BATTINO, R., RHAMY, R., GERLOCK, J. and HOLLIFIELD, J., 1979. Localisation of aldosterone-producing adenoma by computed tomography. *Journal of Clinical Endocrinology and Metabolism, 49*, 642–645.

MITTY, H. A., NICOLIS, G. L. and GABRILOVE, J. L., 1973. Adrenal venography: Clinical-roentgenographic correlation in 80 patients. *American Journal of Roentgenology, 119*, 564–575.

MONTAGNE, J. P., KRESSEL, H. Y., KOROBKIN, M. and MOSS, A. A., 1978. Computed tomography of the normal adrenal glands. *American Journal of Roentgenology, 130*, 963–966.

REUTER, S. R., BLAIR, A. J., SCHTEINGART, D. E. and BOOKSTEIN, J. J., 1967. Adrenal venography. *Radiology, 89*, 805–814.

PHILIPS, 1978. *X-ray scanning: 8: Principles of Computed Tomography.* (Philips Medical Systems, Eindhoven).

SAMPLE, W. F., 1977. A new technique for the evaluation of the adrenal gland with grey scale ultrasonography. *Radiology, 124*, 463–469.

SCHANER, E. G., DUNNICK, N. R., DOPPMAN, J. L., STROTT, C. A., GILL, J. R. and JAVADPOUR, N., 1978. Adrenal cortical tumours with low attenuation coefficients. A pitfall in computed tomography diagnosis. *Journal of Computer Assisted Tomography, 2*, 11–15.

STARER, F., 1965. Percutaneous suprarenal venography. *British Journal of Radiology, 38*, 675–681.

SUTTON, D., 1975. *Textbook of Radiology*, (2nd edit.) (Churchill Livingstone, Edinburgh/London/New York) pp. 856–872.

Book review

Diagnostic Imaging of the Kidney and Urinary Tract in Children. By A. R. Chrispin, I. Gordon, C. Hall and C. Metreweli, pp. xviii+206, 418 illus., 1980 (Current Diagnostic Pediatrics series) (Springer, Berlin/New York), DM.118/$69.70.

ISBN 3-540-09472-5

Infants and children with urinary tract disease present unique problems in diagnosis and management. The rapid proliferation of radiological techniques has increased both the potential for accurate assessment and the complexity of choice for each patient. A detailed review of the subject by four established and respected experts will be welcomed by all, whether regularly or only occasionally concerned with the investigation of the young.

This well-produced slim volume, in hard cover, is the fourth of a series devoted to "Current Diagnostic Pediatrics". After chapters discussing "the clinical context" and "investigatory techniques" there are 11 largely grouped around presenting problems. The role and relative value of each method of investigation is evaluated for each group of presenting problems. Differential diagnostic considerations and management problems are reviewed in some detail. There is an adequate index and ample apt references are appended to each chapter. Most of the profuse illustrations are reproduced to a high standard.

The four authors have achieved a uniform high standard of text which explains the distinct problems of paediatric practice and excites the interests of the reader. There is, perhaps, a relative deficiency of some of the main course after an outstanding aperitif has whetted the appetite. Three examples will suffice. The section discussing the dose of radiopharmaceutical refers to a linear graph of surface area plotted against dose but this is not illustrated nor quantified, leaving the reader in some doubt regarding the dose to be used. After a bold claim in the preface that probabilities are are insufficient for diagnosis, certainty being an essential prerequisite for management, tumefactive xanthogranulomatous pyelonephritis is dismissed as a mass lesion necessitating exploration and excision. Most striking is the unsupported statement "For a serious vasovagal attack following an injection of contrast medium it is possibly not wise to give intravenous atropine". It is to be hoped that any second edition will be expanded to include more substantial fare.

This book will prove to be an invaluable addition to the libraries of all teaching units of radiodiagnosis and paediatrics and should be available in all departments with an occasional need to investigate infants or children.

J. ROYLANCE.

1981, *British Journal of Radiology*, *54*, 1044–1052

The value of transfontanellar ultrasound in infants

By K. C. Dewbury, B.Sc., M.B., B.S., F.R.C.R. and R. I. Bates, R.G.N., M.B., Ch.B.
Radiology Department, Southampton General Hospital

(*Received June 1981*)

ABSTRACT

We report here our experiences over the past two years of using transfontanellar ultrasound to image the infant brain. A consecutive series of 150 examinations has been analysed retrospectively, with particular reference to the clinical indications and accuracy of the technique. Correlation with computed tomography (CT) has been found to be excellent, and the availability of ultrasound has led to a reduction in the proportion of patients receiving CT scans. Ultrasound has directly influenced clinical management and has emerged as the primary imaging procedure for the brain in infants under three months of age.

Until recently, the most widely accepted method for evaluating intracranial abnormalities in infants has been computed tomography (CT). The possibility of demonstrating the brain with B-mode ultrasound has been recognized for some years (De Vleiger *et al.*, 1963). The first detailed cross-sectional demonstration of the infant brain using ultrasound was reported by Kossoff *et al.* (1974) using an automated water path scanner. Kossoff and his co-workers were able to image the brain of infants up to two years of age in considerable detail. The importance of this as an imaging technique was not widely appreciated initially, and it has only been in the last two years that a considerable resurgence of interest in B-mode ultrasound of the infant brain has developed (Pape *et al.*, 1979; Skolnik *et al.*, 1979). Since we first described the technique of transfontanellar ultrasonography (Dewbury and Aluwihare, 1980) this appears to have become the preferred technique both with static and real-time equipment (Edwards *et al.*, 1981; Sauerbrei *et al.*, 1981; Slovis and Kuhns 1981; Grant *et al.*, 1981). We have been using this technique for nearly two years and report a retrospective analysis of 150 consecutive scans performed during this time.

TECHNIQUE

(a) *Static equipment*

Static B-scanners are not freely mobile and it is therefore necessary for the infant to be brought to the equipment. Many of the infants for examination are very ill, and the scanning room should therefore be equipped with oxygen and suction outlets, so that life support measures can be maintained as necessary. Alternatively the infants may be moved in special care incubators with integral life support systems and this has generally been our practice. The maintenance of an adequate body temperature of the neonate is of great importance, and a radiant heat lamp may be necessary for this purpose, even though a full examination will only take between five and ten minutes.

Sedation is never indicated for this examination, but infants are best examined soon after feeding. An oral "dummy" may be helpful if the child is restless. The infant is placed on the examination couch, propped against a pillow in a semi-sitting position, with the head gently supported by a nurse. Small amounts of movement during the examination do not interfere unduly with the diagnostic quality of the images.

The anterior fontanelle varies in size from one infant to another, diminishes in size with age and is rarely more than 2 cm wide. In order to optimize the resolution and the value of this bone-free window, a small diameter transducer is used with the highest possible frequency consistent with obtaining penetration to the full depth of the brain. For the past two years we have been using a 5 MHz transducer with short, internal focus and a flat face of 6 mm diameter. This provides good access and resolution, combined with adequate penetration (although beam spread may become apparent in the far field).

For each examination, a series of closely spaced sector scans is made in both the coronal and sagittal planes, the aim being to include as much of the brain as possible on each scan. In general, the larger the fontanelle, the more complete will be the demonstration of the brain. A more limited access may also be possible through the posterior fontanelle and this may be of value in further evaluation of the posterior fossa. Each image is recorded on some form of hard copy film, with markers placed on the images so that the ventricular size and ratio can be measured following the examination.

(b) *Real time equipment*

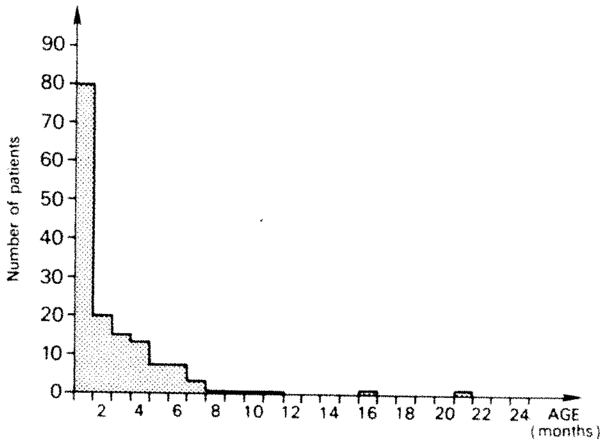
Real time scanners are almost always freely mobile, and so may be taken to the neonatal wards, thus removing the need to transport sick infants to

---

Address for reprints: Dr. K. C. Dewbury, Radiology Department, Southampton General Hospital, Southampton SO9 4XY.

the radiology department. There are two main groups of widely available real time equipment: the linear array and the mechanical sector scanner. In general, the linear array transducer assembly is rather large and this limits access through the anterior fontanelle. High-frequency transducers with much smaller dimensions are now becoming available, and allow better access (Sauerbrei *et al.*, 1981), though their field of view is limited. There can be little doubt that the better alternative for this examination is a high-resolution sector scanner. Factors to be considered in choice of equipment include the size and weight of the transducer assembly and the vibration generated from the motor. A small, light, high-frequency transducer with low vibration is the best choice. The technique for obtaining the images is the same in principle as described for static scanning, but the procedure is quicker and easier. Movements of the baby's head during the examination can be more easily compensated for and are therefore of little consequence. The mobility of the equipment and the speed and ease of use combine to make real time ultrasound an almost ideal modality with which to examine these infants. At the present time, the resolution of static images is superior to real time images, but this is an ever-narrowing gap.

AGE RANGE OF BRAIN SCANS - ULTRASOUND
MAY 1979 — FEB. 1981 (UNDER 2 YEARS)



AGE RANGE OF BRAIN SCANS - C.T.
MAY 1979 — FEB. 1981 (UNDER 2 YEARS)

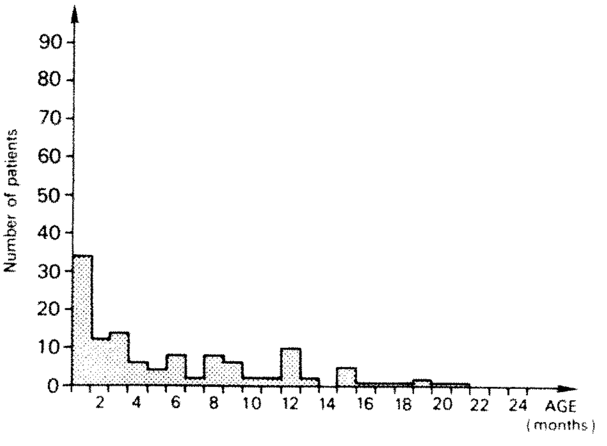


FIG. 1.

Histograms showing the age distribution of infants under two years having ultrasound brain scans and CT brain scans.

PATIENTS AND INDICATIONS

Between May 1979 and March 1981, a total of 150 ultrasound scans of infant brains were performed on a consecutive series of 123 patients. All patients were referred by either paediatric surgeons (63 patients) or paediatric physicians (60 patients) because of clinically suspected intracranial pathology. No scans were performed on clinically normal infants. The age range of patients in this series was 0–21 months, but the majority of patients were under six months of age (Fig. 1). Comparison of ultrasound brain scans with CT in infants under two years shows a more even spread over the age range for CT scans. In only four patients, all early in this series, was CT performed before ultrasound. In the majority of patients, ultrasound was the first imaging procedure performed, and the decision as to whether to proceed to CT was taken with a knowledge of the ultrasound findings.

Neonatal intracranial problems most commonly present in one of the following ways, or as a combination of several.

(a) Raised intracranial pressure. This may be produced by a number of conditions, including hydrocephalus, intracranial haemorrhage, a brain tumour or an abscess.

(b) Seizures and apnoeic attacks. In the neonate, the most likely causes include intracranial haemorrhage, metabolic abnormality, such as hypoglycaemia, neonatal tetany and hypoxia, and infective episodes, such as meningitis and encephalitis.

(c) Central nervous system malformations. The most obvious of these are encephalocele and meningocele, which are frequently associated with hydrocephalus.

(d) Shock syndromes. In the neonate, both severe systemic infections and intracranial infections may cause severe shock.

By far the most common problems requiring confirmation or exclusion are hydrocephalus and intracranial haemorrhage, and these are the major indications for an ultrasound scan in the neonatal period. Our own preliminary experience (Dewbury and Aluwihare, 1980) and, more recently, the work of other groups (Babcock *et al.*, 1980; Edwards *et al.*, 1981; Slovis and Kuhns, 1981; Grant *et al.*, 1981) has indicated that ultrasound reliably and accurately demonstrates the size of the ventricles and also shows the presence of intracerebral haemorrhage. Hydrocephalus may result from congenital malformations. Haemorrhage into the ventricles or subarachnoid space may also cause hydrocephalus. It may develop following intra-uterine infections, such as toxoplasmosis. The definitive surgical management of hydrocephalus is to perform a shunt procedure. The success of the procedure, and the early complications, may be monitored by ultrasound.

The incidence of intracerebral haemorrhage is considerably increased in premature infants (Bernstein *et al.*, 1979). With the growth of high risk nurseries, allowing the survival of very premature infants, this complication is increasingly frequently seen and needs evaluation. The diagnosis of both intracerebral and intraventricular haemorrhage may be made with ultrasound. The blood clots initially produce densely reflective echoes. Intracerebral haemorrhage frequently occurs in the neonate in the sub-ependymal layer in the region of the caudate nucleus. If extensive, the haemorrhage may rupture into the ventricular system from this site. This is a serious complication often leading to hydrocephalus.

RESULTS

In this consecutive series of 123 patients there were no scan failures included. During the past two years, in only one infant has the examination had to be abandoned. There were 78 normal scans (in 75 patients) and 72 scans showing abnormality (in 48 patients). Ultrasound is able to show the normal brain structure in considerable detail, and this is described below with representative sections.

The first is a coronal section (Fig. 2) through the bodies of the lateral ventricles. The ventricles are identified as symmetrically placed fluid-filled structures either side of the mid-line. Between them, the cavum septum pellucidum is seen. In the neonate, and especially in the premature infant, the cavum septum pellucidum may be prominent. It usually disappears during the first year of life, but may be present in up to 25% of infants up to three months of age (Shaw and Alvord, 1969). The cerebral tissue is represented by low and mid-level echoes. Interspersed in these are higher-level echoes corresponding to the sulci and vascular structures. The temporal lobes can be identified, separated from the

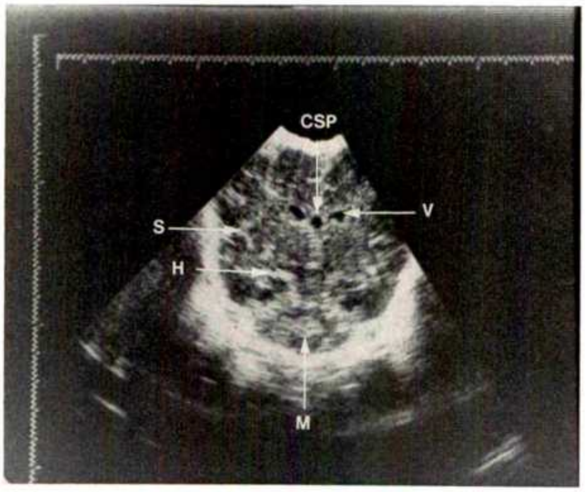


FIG. 2.

A coronal section taken at the level of the bodies of the lateral ventricles. The ventricles (V) are identified as symmetrically placed fluid-filled structures either side of the mid-line. The fluid-filled structure lying between them is the cavum septum pellucidum (CSP). The Sylvian fissure (F) and the hippocampal gyri (H) are identified as relatively echogenic structures within the brain tissue. The midbrain and the pons (M) also have a more reflective pattern than the cerebral cortex.

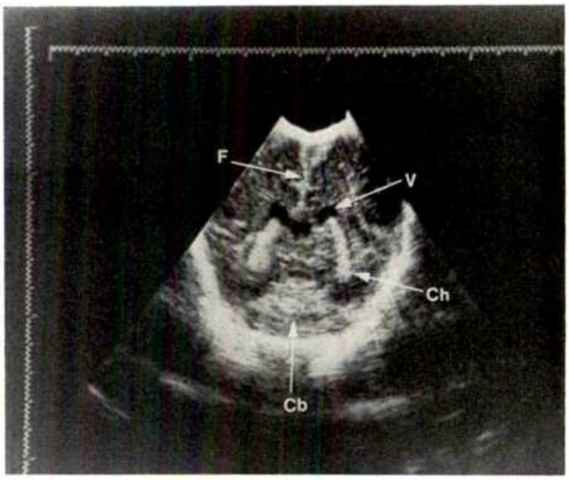


FIG. 3.

A more posteriorly angled coronal section in the same patient through the atria of the lateral ventricles. The highly reflective choroid plexus (Ch) can be seen in the ventricles (V) diverging away from the mid-line as they pass posteriorly. The mid line structures (S) and the echogenic cerebellum (Cb) are also clearly shown.

mid-brain and the pons by the hippocampal gyri which are relatively echogenic. The Sylvian fissures are shown as C-shaped echogenic structures above the temporal lobes. If the transducer is directed at the Sylvian fissures, the pulsations from the middle cerebral arteries can be clearly identified and, if necessary, recorded using the TP mode.

On a more posterior coronal section (Fig. 3) through the atria of the lateral ventricles, choroid plexus can be seen on each side as the strong echogenic structures diverging away from the mid-line. This echo texture is presumably due to the sponge-like configuration of the plexus, producing multiple reflecting interfaces. Posteriorly the segmental shape of the cerebellum is seen, differentiated from the cerebral cortex by its echogenic pattern, and separated from the temporal lobes by the tentorium cerebelli.

Because of the symmetry of the brain, coronal sections are particularly valuable for detecting focal abnormalities such as areas of haemorrhage or infarction. In the next section (Fig. 4), which is a mid-line sagittal section, detail of the normal cerebral sulci is well seen. The cingulate sulcus and a cavum septum pellucidum are identified. Below this, detail of the normal third ventricle is shown. The normal third ventricle may not always be identified, presumably because it is narrow and its walls are parallel to the ultrasound beam. The normal fourth ventricle is less often seen. However, its position can be inferred from the characteristic bright echo patterns of the cerebellum lying posterior to it. In an angled sagittal section it is often possible to outline the major portion of the lateral ventricle in a single sweep (Fig. 5). The echogenic choroid plexus can be seen at the atrium of the ventricle just above the origin of the temporal horn. The thalamic nucleus is shown below the curve of the ventricle, and below this the sella is outlined.

The results can be considered under three categories, according to the original primary clinical indication:

1. *Suspected hydrocephalus—79 cases*

Ultrasound was considered normal in 43 patients. CT was performed in ten of these and also reported normal. In the remaining 33 in this group, follow-up has been by clinical examination, and in no case is there now evidence to suggest hydrocephalus.

Hydrocephalus was demonstrated by ultrasound in 36 patients. This was confirmed by CT in 22 patients, and by air ventriculography in one patient. The mean width of the lateral ventricle in neonates measured at the level of the bodies of the ventricles is 10 mm. It is our practice to consider ventricular ratios of over 30% as abnormal (Johnson *et al.*, 1979). Some caution is, however, necessary in regard to the measuring point, as the occipital horns may often enlarge first in hydrocephalus, producing non-uniform ventricular dilatation. The frequency

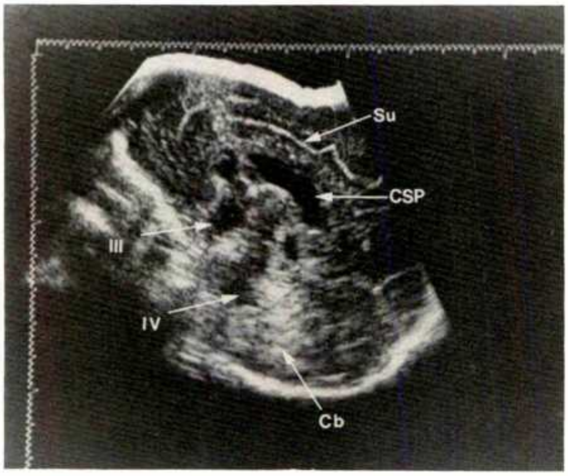


FIG. 4.

Mid-line sagittal section. Detail of the cerebral cortex and cerebral sulci (Su) is well shown. A cavum septum pellucidum (CSP) is present. Below this both the IIIrd ventricle (III) and the IVth ventricle (IV) can be visualized. The cerebellum (Cb) stands out clearly as a more echogenic structure than the cerebral cortex.

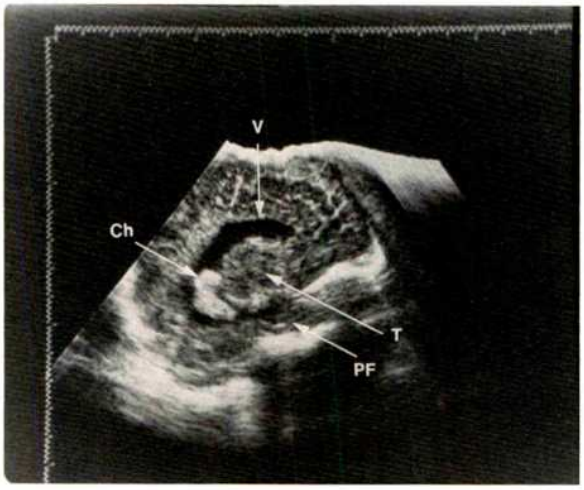


FIG. 5.

An angled sagittal section outlining the major portion of one lateral ventricle (V). The highly reflective choroid plexus (Ch) can be seen at the atrium of the ventricle. Enclosed in the sweep of the ventricle is the nucleus of the thalamus (T) and below this the pituitary fossa (PF) is shown.

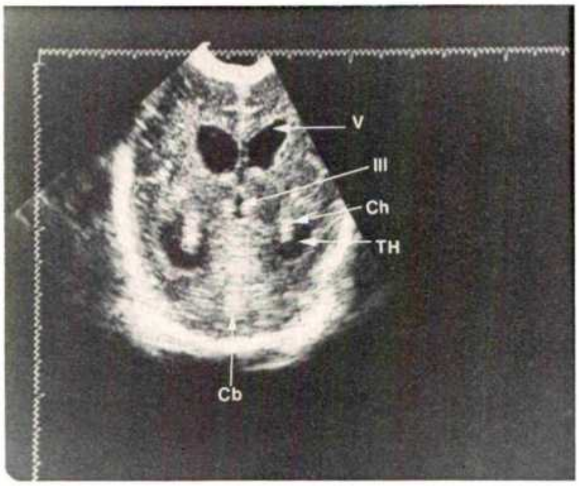


FIG. 6A.

A coronal section in a patient with moderate hydrocephalus. The dilated lateral ventricles (V) stand out clearly. The ventricular ratio is 40%. The third ventricle (III) and the temporal horns of the lateral ventricles (TH) are also identified. The choroid plexus (Ch) can be seen just projecting into the origins of the temporal horns. The cerebellum (Cb) is identified posteriorly.

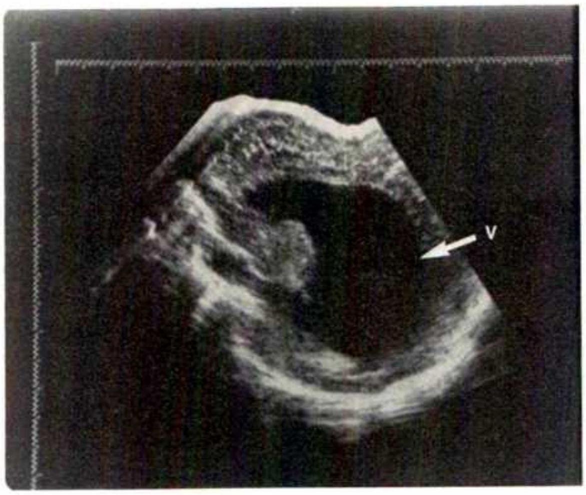


FIG. 6B.

A sagittal section in the same patient. A large part of one lateral ventricle (V) is included on this image. The full extent of the hydrocephalus can be more readily appreciated as the dilatation of the posterior part of the lateral ventricle is disproportionately great.

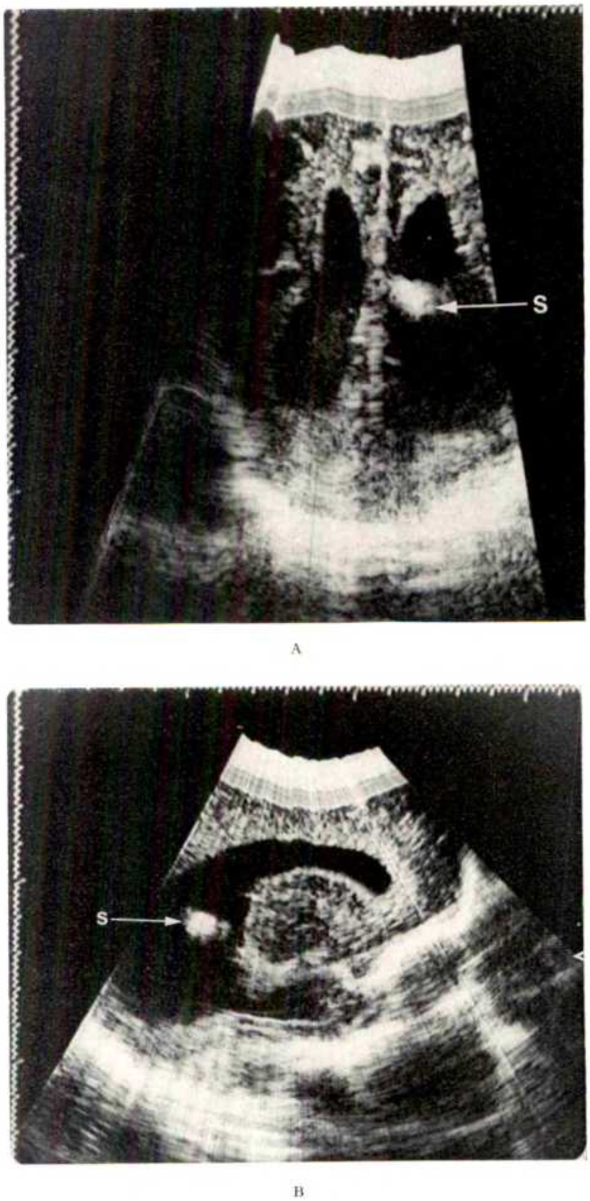


FIG. 7.

(A and B) Coronal and sagittal sections in a patient with a shunt catheter (S) placed in the right lateral ventricle. The ventricles remain considerably dilated for several days after the shunt procedure, suggesting a blockage of the shunt. The fuzzy irregular margins to the catheter tip represent masses of choroid plexus blocking the catheter.

with which this is seen makes it of some importance to image the occipital horns, as they are probably the most sensitive indicator of early hydrocephalus. The sagittal sections are particularly useful in this respect. In borderline cases of hydrocephalus, the shape of the lateral ventricles in coronal sections may also provide a useful clue if the ventricular outline is rounded. An example of moderate hydrocephalus is shown in Fig. 6, where disproportionate enlargement of the occipital horn is seen in the sagittal

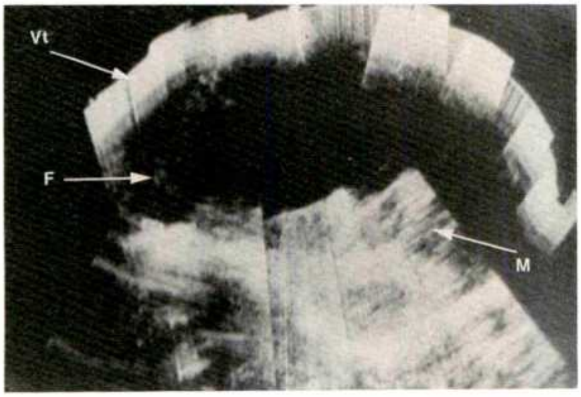


FIG. 8.

A sagittal section showing hydranencephaly. No brain tissue is identified above the mid-brain (M). Between the skull vault (Vt) and the mid-brain, the skull is filled with fluid (F).

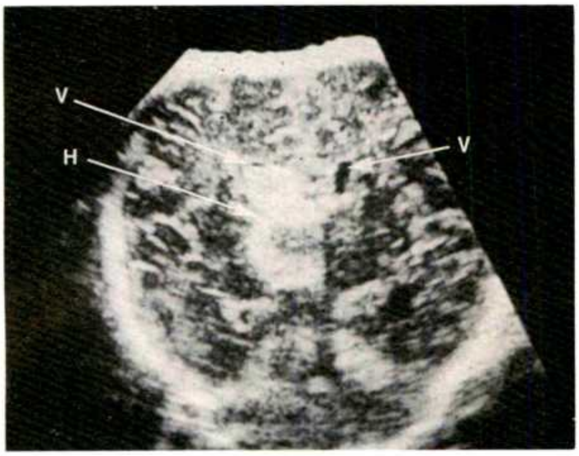
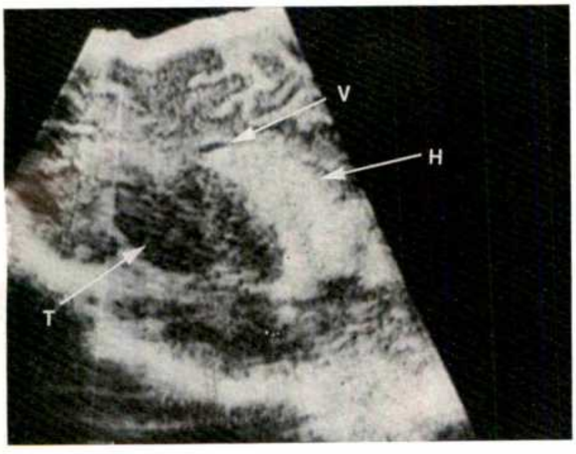


FIG. 9A.

A coronal section showing intracerebral haemorrhage (H) at a characteristic site in the neonate. The haemorrhage is large and is elevating and distorting the lateral ventricle (V) on the side of the haemorrhage. The normal lateral ventricle is clearly seen on the other side.



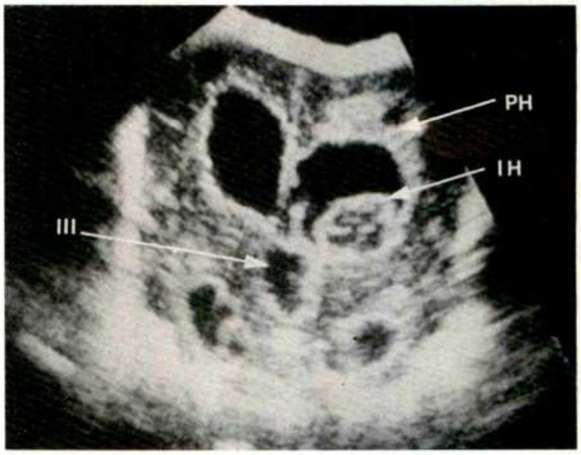


FIG. 10A.

A coronal section in a patient showing periventricular haemorrhage (PH) and intraventricular haemorrhage (IH). The ventricles are markedly dilated and the third ventricle (III) is identified below the dilated lateral ventricles. An area of breakdown is occurring within the periventricular haemorrhage.

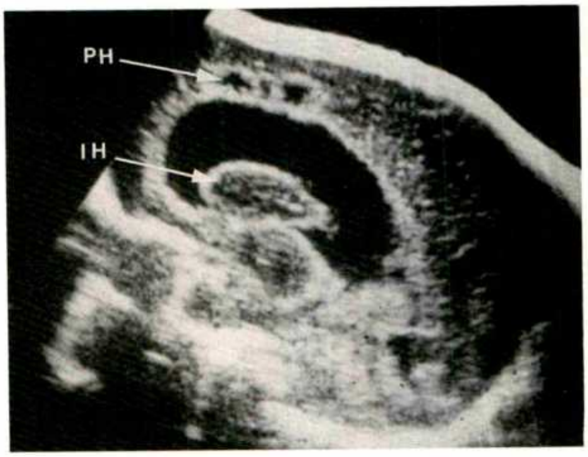


FIG. 10B.

A sagittal section in the same patient again showing both the periventricular haemorrhage (PH) and the intraventricular haemorrhage (IH). The central breakdown in the periventricular haemorrhage can be more readily appreciated on this sagittal section.

FIG. 9B.

Sagittal section in the same patient showing the classical distribution of the haemorrhage (H) in the region of the caudate nucleus. The reflective area of haemorrhage clearly outlines the posterior part of the thalamic nucleus. The compressed ventricle (V) can just be seen above the caudate nucleus haemorrhage.

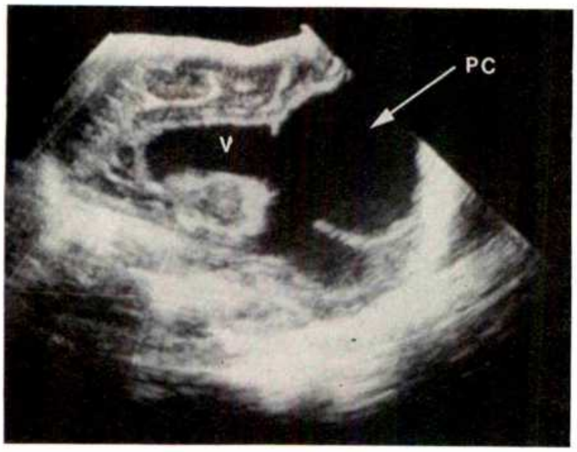


Fig. 11.
A sagittal section showing a large occipital porencephalic cyst (PC) in continuity with the posterior part of the lateral ventricle. This cyst was secondary to a documented cerebral infection.

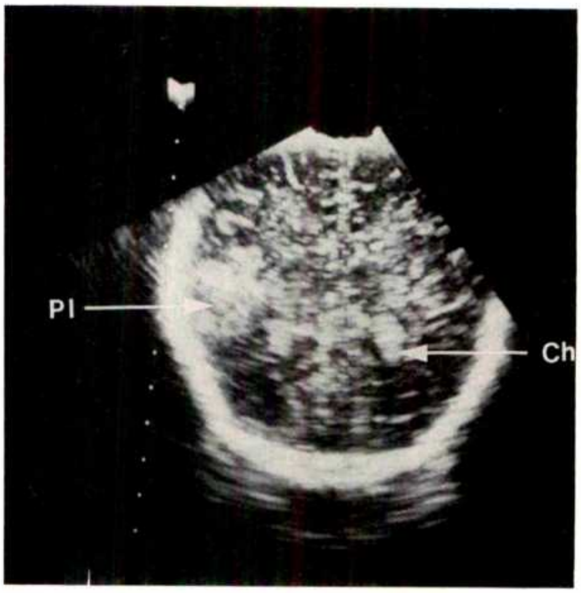


Fig. 12.
A posteriorly angled coronal section showing a localized parietal infarct. The ultrasound appearances are initially those of an area of localized haemorrhage. The choroid plexus (Ch) can be identified.

section. The correlation in regard to ventricular size on CT and ultrasound is almost exact. In the remaining 13 patients in this group with hydrocephalus, CT was not performed, but either a shunt procedure was performed on the basis of the ultrasound findings, or the patient died as a result of a positive decision not to perform a shunt.

Following insertion of a ventricular shunt, ultrasound is able to show the position of the catheter tip. The ventricular size can be closely monitored and complications such as haemorrhage may be demonstrated. Shunt blockage due to masses of choroid plexus around the catheter may also be shown (Fig. 7).

Within this full group of 79 patients, 21 patients had a neural canal defect of some type, and of these 16 were shown to have hydrocephalus, an incidence of 76%. Under half this number were clinically suspected of having hydrocephalus. In addition to hydrocephalus, other cystic abnormalities in the head are readily demonstrated by ultrasound, and included in this group was one case of hydranencephaly (Fig. 8). In this situation, no cortical tissue is identified above the mid-brain.

2. *Suspected intracranial haemorrhage—38 cases*

Ultrasound was considered normal in 30 patients; of these, four patients had CT scans which were also normal, and the remaining 26 have been carefully followed by clinical examination. To date, there is no evidence of any false negative ultrasound studies in this group. In eight patients, ultrasound showed evidence of periventricular haemorrhage (Fig. 9) or intraventricular haemorrhage (Fig. 10). The characteristic appearance of haemorrhage on ultrasound is as an echogenic mass. Intraventricular haemorrhage must be distinguished from the normal choroid plexus which unlike haemorrhage, is attached medially to the ventricular atrial wall. At present it is not clear how soon after bleeding a ventricular clot will become echogenic, and so be visualized by ultrasound; but Slovis and Kuhns (1981) report a case seen two days after birth. In time, areas of intracerebral haemorrhage may show evidence of central breakdown (Fig. 10) and it is possible that it is at these sites that a porencephalic cyst may develop. This cystic abnormality has a very characteristic ultrasound appearance of a rounded fluid-filled structure in continuity with the ventricle (Fig. 11). In four of the eight patients, the ultrasound findings were confirmed by CT. In two patients, follow-up ultrasound showed the development of hydrocephalus, later confirmed in both cases by CT. The case history of one of these patients has been described previously (Dewbury and Aluwihare, 1980). The other two patients died. The presence of extensive germinal layer haemorrhage was confirmed in one at post-mortem. The other patient did not have a post-mortem and the ultrasound diagnosis therefore remains unconfirmed.

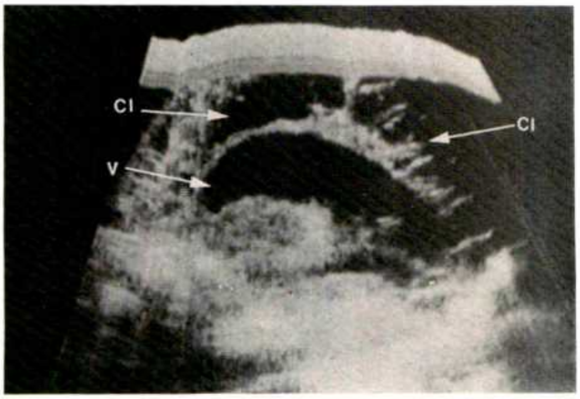
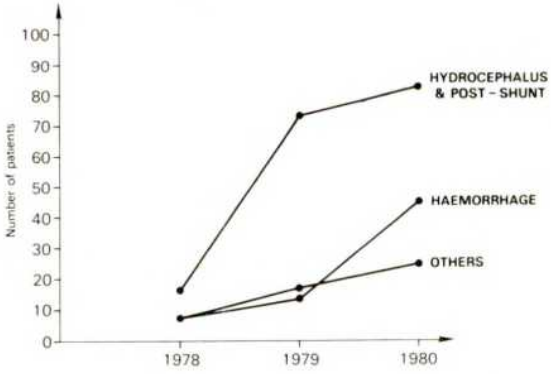


FIG. 13.

A sagittal section showing extensive cortical infarction (CI). Much of the cortex appears to have disappeared and is replaced by lakes of fluid. The lateral ventricles (V) are also dilated.



(OTHERS = P. U. O., Post - Meningitis etc.)

FIG. 14.

Total paediatric neurological referrals for brain scan according to clinical indication (up to two years old).

3. *Other categories—six cases*

This group is a mixture of different pathologies. Two patients showed a localized brain infarct, both by ultrasound and CT (Fig. 12). The ultrasound appearances are those of a localized haemorrhage, and distinction from a brain tumour is probably not possible. The follow-up CT scans showing the resolution of the lesion establish the diagnosis of an infarct. Another patient showed extensive brain infarction with both techniques, where the cerebral cortex appears to be partially replaced by lakes of fluid (Fig. 13). In one case a diagnosis of tuberose sclerosis was made at CT, where the ultrasound only demonstrated moderate ventricular dilatation. In another patient who had normal ultrasound and CT studies, post-mortem diagnosed the Werdnig-Hoffmann syndrome. Finally, there was one patient with a cephalhaematoma for whom both ultrasound and CT studies were normal.

Both ultrasound and CT scans were performed on 48 patients. Excluding minor degrees of cortical atrophy, which was suggested by CT in nine patients, there was correlation with ultrasound in 47 patients (98%). The other patient had tuberous sclerosis. A large prospective study, rather than a retrospective study such as this, is probably essential to assess fully the accuracy of ultrasound and its limitations in relation to CT. However, it is clear that our experience regarding its accuracy agrees with the experience of other workers.

DISCUSSION

In the past two years, the technique of transfontanellar ultrasound of the infant brain has evolved as a major new application of ultrasound. It has a high degree of accuracy in demonstrating both hydrocephalus and intracerebral haemorrhage with excellent correlation with CT. Ultrasound is a non-invasive technique, and, in the form of real time equipment, it provides a nearly ideal diagnostic tool. However, if ultrasound is to make a really significant contribution to the management of this group of patients it must be able to replace existing procedures rather than simply complement them. We have analysed all the paediatric neurological brain scan referrals over the past two years, according to clinical indication (Fig. 14) and according to imaging procedure performed (Fig. 15). There has been a dramatic increase in the number of patients referred either with suspected hydrocephalus or suspected haemorrhage. This is almost exactly mirrored by the number of ultrasound studies performed. The rise in the number of CT scans being performed in the same period is only modest, particularly in infants under three months of age. This is at a time when the overall demand for brain CT has risen dramatically. In addition, late in 1978, a change was made in the practice of infants having a general anaesthetic for a CT scan to a heavy sedation regime. This change alone was expected to increase substantially the demand for CT in this age group. We conclude that these observations indicate a substantial relative reduction in the number of CT scans being performed over this short time. It is our opinion that this trend will continue as ultrasound equipment improves and as our experience grows. We have attempted to assess the clinical impact of ultrasound by retrospective analysis of the patients' records. Of

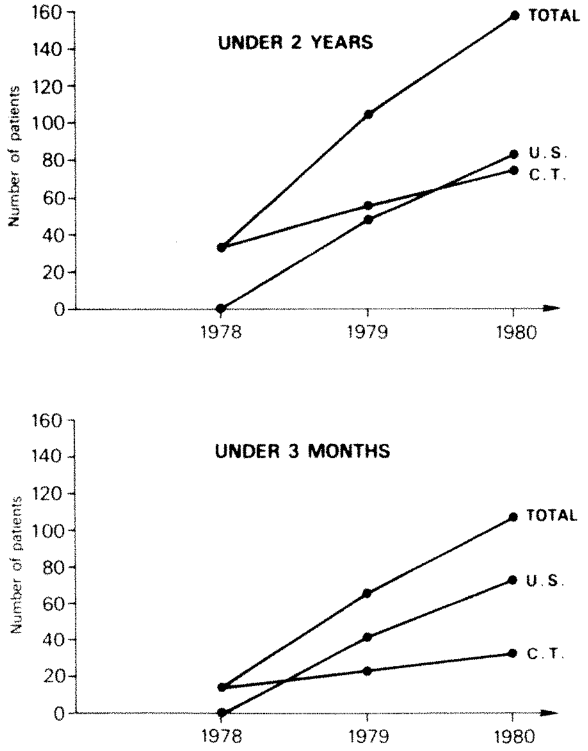


FIG. 15.

Total paediatric neurological referrals for brain scan according to imaging modality used. The steep rise in the number of referrals is almost exactly mirrored by the number of ultrasound studies being performed, particularly in the under three months age group.

necessity, this remains a little anecdotal, but it appears that the ultrasound result influenced the management in almost every instance, even if only, in some patients, confirming a decision to proceed to CT. More specifically, in 59 patients, no further imaging procedures were performed on the basis of the ultrasound results. The majority of ventricular shunts are now only followed, certainly initially, by ultrasound studies. In eight cases ot hydrocephalus diagnosed by ultrasound, six were not shunted and two were shunted on the basis of the ultrasound findings. This means that in over half the patients in this series the result of the ultrasound study has been shown to have a major influence on clinical management.

Ultrasound is, in general, more readily available than CT. Our experience suggests that in certain instances it is able to replace CT, and that overall it has a major influence on clinical management. These three factors point to the use of ultrasound as the primary imaging procedure for the neonatal brain in the future. CT is undoubtedly more accurate than ultrasound in certain conditions, for example, delineation of brain tumours, particularly in the posterior fossa, and the demonstration of subarachnoid haemorrhage. The precise interrelationship between the two techniques remains to be defined.

REFERENCES

BABCOCK, D. S., HANN, B. K. and LE QUESNE, G. W., 1980. B-Mode greyscale ultrasound in the head in the newborn and young infant. *American Journal of Roentgenology*, *134*, 457–468.

BERNSTEIN, J., PAPILLE, L. and BERNSTEIN, R., 1979. Intraventricular haemorrhage and hydrocephalus in premature newborns: a prospective study with CT. *American Journal of Roentgenology*, *132*, 631–635.

DE VLEIGER, M., STERKE, A., DE MOLIN, C. E. and VAN DER VEN, C., 1963. Ultrasound for two-dimensional echo encephalography. *Ultrasound*, *I*, 148–151.

DEWBURY, K. C. and ALUWIHARE, A. P. R., 1980. The anterior fontanelle as an ultrasound window for study of the brain. *British Journal of Radiology*, *53*, 81–84.

EDWARDS, M. K., BROWN, D. L., MULLER, J., GROSSMAN, C. B. and CHUA, G. T., 1981. Cribside neurosonography. *American Journal of Roentgenology*, *136*, 271–276.

GRANT, E. G., SCHELLINGER, D., BORTS, F. T., MCCULLOUGH, D. C., FRIEDMAN, G. R., SIVAS, U., BRAMANIAN, K. N. and SMITH, Y., 1981. Real time sonography of the neonatal and infant head. *American Journal of Roentgenology*, *136*, 265–270.

JOHNSON, N. L., MACK, L. A., RUMAK, C. N., FROST, M. and RASHBAUM, C., 1979. B-Mode echo encephalography in the normal and high risk infant. *American Journal of Roentgenology*, *153*, 375–381.

KOSSOFF, G., GARRETT, W. J. and RADAVANOVICH, G., 1974. Ultrasonic atlas of normal brain of infant. *Ultrasound in Medicine and Biology*, *I*, 259–266.

PAPE, K. E., CUSICK, G., HOUANG, M. T. W., BLACKWELL, R. J., SHERWOOD, A., THORBURN, R. J. and REYNOLDS, E. O. R., 1979. Ultrasound detection of brain damage in pre-term infants, *Lancet*, *i*, 1261–1264.

SAUERBREI, E. E., HARRISON, P. B., LING, E. and COOPERBERG, P. L., 1981. Neonatal intracranial pathology demonstrated by high frequency linear array ultrasound, *Journal of Clinical Ultrasound*, *9*, 33–36.

SHAW, C. N. and ALVORD, E. C. JR., 1969. Cava septi pellucidi et vergi: Normal and pathological states. *Brain*, *92*, 213–224.

SKOLNIK, M. L., ROSENBAUM, A. E., MATZUK, T., GUTHKELCH, A. N. and HEINZ, E. R., 1979. Detection of dilated cerebral ventricles in infants: a correlative study between ultrasound and computed tomography. *Radiology*, *131*, 447–451.

SLOVIS, T. L. and KUHNS, L. R., 1981. Real time sonography of the brain through the anterior fontanelle. *American Journal of Roentgenology*, *136*, 277–286.

1981, *British Journal of Radiology*, 54, 1053–1061

An evaluation of CT systems from ten manufacturers

By *R. D. Speller, Ph.D., †D. R. White, Ph.D., ‡C. K. Showalter, M.S., §L. N. Rothenberg, Ph.D., §K. S. Pentlow, M.Sc., ‖T. J. Morgan, Ph.D. and ‡T. B. Shope, Ph.D.

*Department of Physics as Applied to Medicine, Middlesex Hospital Medical School, Cleveland Street, London W1P 6DB, †Radiation Physics Department, St. Bartholomew's Hospital, 13 Bartholomew Close, London EC1A 7BE, ‡Bureau of Radiological Health, Rockville, Maryland, USA and § Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY., USA

(Received November 1980 and in revised form May 1981)

ABSTRACT

During the past three years, 23 computerized tomography (CT) machines from ten different manufacturers located in Europe and the USA have been evaluated. Using the same set of phantoms and measurement techniques, performance data have been derived including noise, uniformity of CT numbers, low contrast detectability, spatial resolution, modulation transfer function, effective photon energy and linearity of CT numbers. Thermoluminescent and film dosimetry were used to determine single-slice dose profiles at the periphery and centre of specialized anthropomorphic phantoms. The results of this study are presented in tabular and graphical form together with some general conclusions on their implications.

Since the development of the first commercial CT machine in 1972 (Hounsfield, 1973), a large number of systems have been introduced. More than twenty models from over ten different manufacturers have been brought onto the market during this period with varying degrees of success.

The performances of these diverse systems are difficult to assess due to the fragmentary nature of published measurements, often based on rather limited measurement techniques and phantoms. Potential users, unless able to undertake the necessary detailed measurements themselves, are often forced to rely on performance data supplied by manufacturers who, understandably, emphasize the best aspects of their machines, frequently presenting results derived under idealized conditions.

The purpose of this study has been to obtain performance data from the important CT machines, using a single set of regular geometry and anthropomorphic phantoms and common, comprehensive measurement techniques (White *et al.*, 1981). In addition, every effort was made to assess each scanner in a hospital environment, using operating modes in routine clinical use at the hospital being visited. A report on a group of EMI machines (CT1010 and CT5005), using the same phantoms and techniques, has already been published (Speller *et al.*, 1981), and this communication is an extension of the study covering a further 17 types of CT machines.

In order to evaluate so many different machines, installations in both Europe and the USA had to be visited, necessitating the collaboration of three groups of physicists, each responsible for a definite aspect of the study. The logistics of the work undertaken in the USA and the thermoluminescent dosimetry (measurement and analysis) were organised by the Bureau of Radiological Health, Rockville, Maryland (C.K.S., T.J.M., T.B.S.). The Memorial Sloan-Kettering Cancer Center, New York (L.N.R., K.S.P.), undertook all aspects of the film dosimetry.

The UK authors (R.D.S., D.R.W.) were responsible for producing the phantoms and for the measurement and analysis of the radiographic performance data.

THE CT MACHINES SURVEYED

The CT machines evaluated in this study are listed alphabetically according to manufacturer in Table I. Of the machines assessed, 20 were in routine clinical use at the time of the measurements. To observe complete anonymity the exact locations of these 20 machines will not be given. It is perhaps interesting to note that installations in Britain, Holland and the USA were visited, including hospitals in Washington, New York, Cleveland, Indianapolis, St. Louis and Utrecht. The Pfizer A.S. & E. Model 0500 was a factory-based machine, as was one of the four Philips Tomoscan-300 machines. The EMI model CT7070 was installed at a hospital but assessed during its pre-clinical trials.

Table I also gives details of machine type, scanning motion, number and type of detectors. General-purpose machines are classified as "body" scanners, while specialized head machines are referred to as "brain" scanners. Scanning motion is described in three ways. Rotate-Translate (RT) machines are those where the X-ray tube translates and then indexes around the patient. Rotate—Rotate (RR)

‖Present address: Philips Medical Systems Inc., Shelton, CT, USA.

The opinions and statements contained in this paper are those of the authors and may not reflect the views of the US Department of Health & Human Services. The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department.

TABLE I

SOME BASIC PHYSICAL DATA FOR THE CT SYSTEMS SURVEYED

Manufacturer	Model	Type	Scanning motion*	Detectors		Brain scanning				Body scanning			
				No.	Type†	Pixel size (mm)	kV	mA (mAs)	Scan time (sec)	Pixel Size (mm)	kV	mA (mAs)	Scan time (sec)
Pfizer/A.S. & E.	0500	Body	R.S.	600	'crystals'	0.50	125	20	10	1.00	125	50	5
Elscint	WF710	Body	R.T.	52	BGO	1.00	140	29	40	1.56	140	29	10
EMI	MkI	Brain	R.T.	1	NaI	1.50	120	33	390	–	–	–	–
General Electric	CT7070	Body	R.S.	1088	CsI	0.78	120	99	3	1.25	120	25	3
	CT/T7800	Body	R.R.	304	Xe	1.30	120	(152)	4.8	1.30	120	(238)	4.8
	CT/T8800	Body	R.R.	523	Xe	0.78	120	(760)	9.6	1.10	120	(475)	9.6
Ohio-Nuclear	Δ50	Body	R.T.	3	CaF	1.06	120	30	120	1.52	120	30	150
	Δ50FS2	Body	R.T.	12	BGO	0.99	140	35	18	1.68	140	35	18
	Δ190	Brain	R.T.	3	NaI	1.00	120	25	120	–	–	–	–
	Δ2020	Body	R.S.	720	BGO	0.49	120	50	8	0.78	120	100	2
Philips	Tomoscan-200	Body	R.T.	30	BGO	0.90	140	28	64	1.80	140	28	25
	Tomoscan-300	Body	R.R.	288	Xe	0.90	100	150[a]	4.2	1.50	120	250	4.2
Picker	SD600	Body	R.S.	600	BGO	1.20	130	65	4.9	1.52	130	95	6.6
Searle	Photrax 4000	Body	R.R.	504	Xe	1.25	130	30	20	1.56	130	30	5
Siemens	Sireton	Brain	R.T.	16	CsI	1.90	133	30	68	–	–	–	–
	Somatom	Body	R.R.	256	'scintillac'	1.05	125	(230)	38	2.11	125	(60)	4.8
Varian	V360	Body	R.R.	301	Xe	1.84	120	100	3	1.84	120	100	3

[a] Tomoscan-300(4) used 350 mA

*R.T: rotate-translate; R.R: rotate-rotate; R.S: rotate-stationary.

†BGO: bismuth germanate

TABLE II

SUMMARY OF PHANTOMS USED AND MEASUREMENT TECHNIQUES

Parameter	Phantoms used	Measurement techniques
Alignment	Regular geometry—20 cm and 33 cm dia.	Subjective analysis of images of 3.17 mm dia. aluminium pin located centrally.
Slice thickness	Regular geometry—20 cm and 33 cm dia.	Derivation of FWHM from CT number profiles using 30°/45° inclined Al plates, located at top, centre and bottom of phantoms.
Noise	Circular, water-filled Perspex container—20 cm and 33 cm dia.	Standard deviation (σ) of central, circular area, 100 pixel radius, expressed as percentage of difference between CT numbers for water (H_w) and air (H_a), *i.e.* $\frac{\sigma}{H_w - H_a} \times 100(\%)$.
Uniformity of CT numbers	Circular, water-filled Perspex container—20 cm and 33 cm dia.	Maximum difference in CT numbers in 20 pixel radius, circular areas at centre (H_1) and periphery (H_2), expressed as percentage difference between H_w and H_a, *i.e.* $\frac{(H_1 - H_2)_{max}}{H_w - H_a} \times 100(\%)$
Low-contrast detectability	Anthropomorphic skull and thorax	Subjective analysis of images of polystyrene rods embedded in water substitute (2–5% contrast). Minimum detectable dia. rod noted at various locations in the phantoms.
Spatial resolution	Anthropomorphic skull and thorax	Subjective analysis of images of arrays of rods of cortical bone substitute. Minimum detectable dia. noted at central and various other locations in the phantoms.
Modulation transfer function	(1) Regular geometry—20 cm dia. (2) Anthropomorphic thorax	Derived from Perspex edge in water substitute located at various peripheral sites, using the technique of Judy (1976).
Dose received by the patient	Anthropomorphic skull and thorax (Dosimetry Phantoms)	Dose profiles assessed from arrays of TLD and film strips at central and between 6–8 surface locations.
Effective energy and linearity of CT numbers	Regular geometry—20 cm and 33 cm dia	Evaluation based upon 'keV liquids' introduced by White & Speller (1980). All measurements made at central locations.

systems have a rotating X-ray tube and detectors without translation. Rotate—Stationary (RS) machines have a rotating X-ray tube and a stationary bank of detectors. From 1–1088 detectors are used in these systems, including a variety of ionization and solid state devices and scintillation materials.

In Table I information on pixel size (mm), kilovoltage, tube current (mA or mAs) and scan time (sec) is given for brain and body (that is, abdomen, thorax) scanning. The exposure factors represent the normal values employed at the sites visited for the majority of routine clinical investigations. The use of special hardware and software packages for high-resolution reconstructions were not considered in this analysis. It must be stressed that the performance parameters quoted in this paper may differ from those issued by manufacturers where each parameter is estimated after the system has been optimized for such measurements. However, use of the scanning technique factors given in Table I means that the performance data presented here represent typical values that could be expected from these machines when carrying out a radiological examination.

It is also important to realize that in many instances this survey only considered single examples of given scanner types so care must be exercised in assuming these performance data relate to average performances. In the case of General Electric CT/T8800, and Philips Tomoscan-200 and Tomoscan-300 machines, more than one model was assessed.

Of the three surveys on General Electric machines (CT/T8800(1)—CT/T8800(3)), the first two were performed on the same machine, while CT/T8800(2) was surveyed 20 months after CT/T8800(1). Two Philips machines, Tomoscan-200(1) and Tomoscan-200(2) were assessed, the first having experimental collimation although still in use clinically. Four surveys on machines Tomoscan-300(1)—Tomoscan-300(4) included repeat measurements. The first two and the last two were the same models but surveyed after intervals of three and six months respectively.

All systems were calibrated in Hounsfield Units except EMI Mk I and General Electric CT/T7800 which were in EMI Units.

MATERIALS AND METHODS

A range of solid and water-filled phantoms was used in the experimental part of this study.

Regular geometry phantoms were solid, 6 cm thick circular discs of an epoxy-resin-based water

TABLE III

MEASURED SLICE THICKNESS, EFFECTIVE ENERGY (E_{eff}) AND LINEARITY OF CT NUMBERS

Machine		Brain scanning					Body scanning				
		Slice thickness (mm)		E_{eff} (keV)	$\mu = a_1(\text{CT No.}) + a_0$		Slice thickness (mm)		E_{eff} (keV)	$\mu = a_1(\text{CT No.}) + a_0$	
		Nominal	Measured		a_0	a_1	Nominal	Measured		a_0	a_1
Elscint	WF710	12	7.3	73	0.190	1.97×10^{-4}	12	7.8	–	–	–
EMI	MkI	13	–	70	0.193	3.90×10^{-4}	–	–	–	–	–
	CT7070	5	5.8	72	0.188	1.94×10^{-4}	10	12.0	74	0.193	2.28×10^{-4}
General Electric	CT/T7800	10	9.8	71	0.192	4.17×10^{-4}	10	10.0	–	–	–
	CT/T8800(1)	10	9.7	69	0.193	2.02×10^{-4}	10	9.3	70	0.192	2.13×10^{-4}
	CT/T8800(2)	10	10.7	70	0.191	2.04×10^{-4}	10	10.9	72	0.189	1.94×10^{-4}
	CT/T8800(3)	10	11.4	69	0.193	2.22×10^{-4}	10	–	72	0.191	2.00×10^{-4}
Ohio-Nuclear	Δ50	13	7.1	68	0.196	2.04×10^{-4}	13	7.7	70	0.195	2.08×10^{-4}
	Δ50FS2	13	–	74	0.190	1.97×10^{-4}	13	–	77	0.186	1.85×10^{-4}
	Δ190	10	–	66	0.197	2.09×10^{-4}	–	–	–	–	–
	Δ2020	10	9.5	70	0.189	2.05×10^{-4}	10	8.9	–	–	–
Philips	Tomoscan-200 (1)	10	–	74	0.184	1.96×10^{-4}	10	–	–	–	–
	Tomoscan-200 (2)	10	5.9	75	0.188	1.78×10^{-4}	10	9.6	78	0.194	1.97×10^{-4}
	Tomoscan-300 (1)	9	–	68	0.195	1.93×10^{-4}	12	–	72	0.191	2.10×10^{-4}
	Tomoscan-300 (2)	9	9.6	68	0.194	1.94×10^{-4}	12	12.5	72	0.191	2.14×10^{-4}
	Tomoscan-300 (3)	9	–	69	0.192	2.00×10^{-4}	12	–	75	0.187	1.93×10^{-4}
	Tomoscan-300 (4)	9	9.0	–	–	–	12	10.0	–	–	–
Picker	SD600	10	–	75	0.190	1.95×10^{-4}	10	–	79	0.196	2.41×10^{-4}
Searle	Photrax-4000	10	8.0	68	0.192	1.94×10^{-4}	10	5.2	71	0.198	1.88×10^{-4}

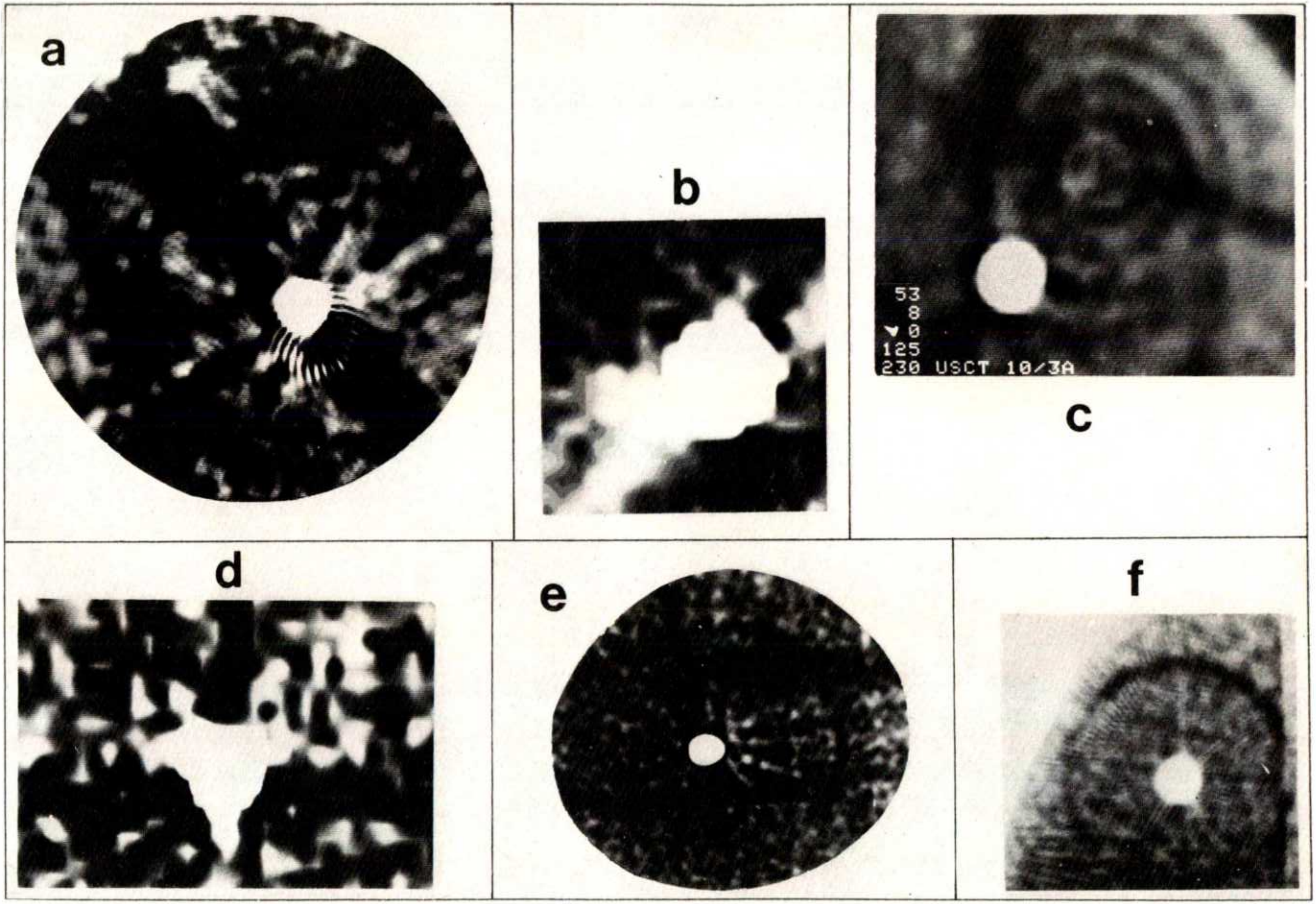


Fig. 1.

CT scans of the aluminium alignment pin from six different machines. a—Picker SD600; b—General Electric CT/T7800; c—Siemens Somatom; d—Ohio-Nuclear Δ50; e—Elscint WF710; f—Varian CT.

TABLE IV

MEAN VALUES AND STANDARD DEVIATIONS (SD) FOR SIX OF THE PERFORMANCE PARAMETERS EVALUATED

Parameter	Brain scanning			Body scanning		
	No. systems	Mean	SD	No. systems	Mean	SD
Noise(%)	19	0.6	0.5	19	0.9	0.5
Uniformity of CT numbers (%)	19	0.6	0.5	19	0.9	0.8
Low-contrast detectability (mm)	23	2.7	1.0	19	3.8	1.0
Spatial resolution (mm)	23	1.5	0.3	20	1.8	0.4
MTF (50% cut-off) (cycles. cm^{-1})	7	2.4	0.6	6	2.0	0.4
Max. surface dose (mGy)	22	30	23	19	23	14

substitute. Two types were available. A 20 cm diameter disc with a 4 mm ring of cortical bone represented the skull, while a 33 cm disc represented the abdomen.

Anthropomorphic phantoms, 6 cm thick, composed of epoxy-resin-based tissue substitutes, included skull, upper abdomen and mid-thorax sections.

Dosimetry phantoms were solid, anthropomorphic in design with central and surface channels for thermoluminescent and film dosemeters. In use the dosimetry phantoms were sandwiched between two 5 cm thick "scatter" blocks of Plexiglas.

Water-filled Perspex containers were also used. Two circular containers both 10 cm thick, 20 cm and 33 cm diameter, represented the skull and abdomen respectively.

The solid regular-geometry and anthropomorphic phantoms had cavities into which conical plugs could be inserted. The plugs contained test pieces enabling all the important CT performance parameters to be readily measured. The design and philosophy behind these phantoms have recently been reported (White *et al.*, 1981).

Nine performance parameters were evaluated, namely: Alignment, Slice thickness, Noise, Uniformity of CT number, Low-contrast detectability, Spatial resolution, Modulation transfer function, Dose received by the patient, Effective energy and linearity of CT numbers.

A summary of the phantom arrangements used during the study and the measurement techniques adopted for the evaluation of these parameters is given in Table II. Throughout the study, brain scanning was evaluated with 20 cm diameter regular-geometry or anthropomorphic skull phantoms; body scanning was assessed with the 33 cm diameter regular-geometry and the anthropomorphic abdomen or thorax phantoms. A fuller discussion of these procedures is to be found in the earlier publications of White *et al.* (1981) and Speller *et al.* (1981).

RESULTS

The main results of this evaluation are presented in Tables III and IV and Figs. 1 and 2. Because of deficiencies in hardware and software with certain models, such as lack of line-printer, statistical packages, etc., it was not possible to obtain a full set of performance data for each machine. Consequently omissions are apparent in some of the data presented.

Alignment. One system produced significant streaking around images of the high contrast aluminium pin, indicating poor mechanical alignment. Other artefacts liable to be confused with diagnostic information were noted on a number of machines. Some examples of these are shown in Fig. 1 and include ring artefacts and various structured imaging defects.

Slice Thickness. Nominal (as supplied by manufacturers) and measured slice thickness are shown in Table III. The measured values are means from estimates at the top and centre or top and bottom of the phantom, depending upon scanning motion. Poor correlation between nominal and measured values was noted for a number of systems.

Noise. These results for the machines surveyed are presented in the top graphs given in Fig. 2, with brain scanning shown on the left and body scanning on the right. Noise is generally between 0.2 and 1% for brain scanning, with many machines below or equal to 0.5%. A wider spread of increased noise values was apparent with body scanning, namely 0.3–2%.

Uniformity of CT numbers. These data are plotted on the same axes as noise (top graphs, Fig. 2). In a number of instances the uniformity data are seen to approach and exceed the noise values. Under these conditions the non-uniformity would be visible in scans viewed at normal window and level settings. Brain scanning appeared to suffer more from this problem than body scanning.

Low-contrast detectability. The results for this parameter are shown in the second set of graphs from

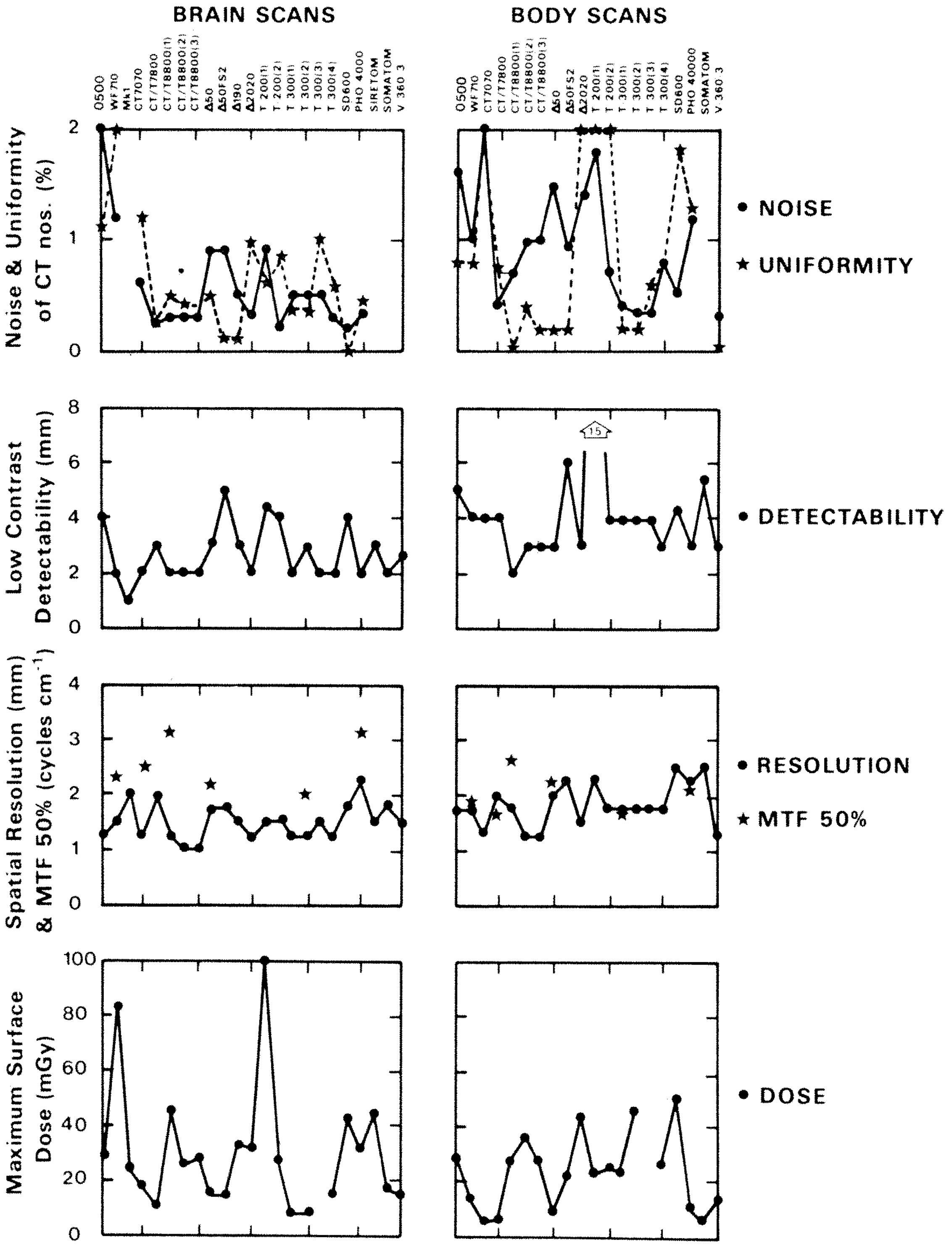


FIG. 2.

Graphical representation of noise, uniformity of CT numbers, low-contrast detectability, spatial resolution, MTF (50% cut-off) and maximum surface dose.

the top in Fig. 2. It can be seen that many machines had minimum detectable diameters between 2—4 mm for brain scanning and 3–4 mm for body scanning. An inspection of the relevant graphs in Fig. 2 will indicate a reasonable correlation between the subjective measurement of low contrast detectability and the objective parameter, noise. That is, an increase in the noise corresponds with an increase in the diameter of the minimum detectable polystyrene rod. No corrections have been made for the different beam energies used and the corresponding change in the contrast of polystyrene compared with water.

Spatial resolution. The results for spatial resolution are plotted in the second set of graphs from the bottom of Fig. 2, and showed a remarkable consistency considering the diversity of the machines being tested. As expected, brain scanning gave slightly better resolution values of between 1–2.25 mm compared to body scanning which was 1.25–2.5 mm. The results correlate well with the pixel sizes given in Table I.

Modulation transfer function (MTF). The spatial frequency at which the MTF, derived from an edge response, falls to 50% is plotted for each machine on the same axes used for spatial resolution (Fig. 2, second set of graphs from bottom). Brain scanning produced frequencies predominantly in the range 2–3 cycles. cm^{-1}, while body scanning yielded values $\sim$ 2 cycles. cm^{-1}. The lack of print-out facilities at several centres visited is the reason for the reduced number of MTF values plotted here, making any correlation between MTF and any other parameter such as spatial resolution difficult to positively identify.

Dose received by the patient. A wide variation in dose to the patient, particularly for brain scanning, is evident from the plotted maximum surface dose data shown in the lower graphs of Fig. 2. For single slices in brain scanning, maximum surface doses from 10–100 mGy were recorded. These corresponded to maximum surface body doses, again for single slices, of 6–50 mGy. In general, an increase in dose is seen to be reflected in lower noise values and improvement in low-contrast detectability. A more detailed account of the dosimetric aspects of this study, including the presentation of complete single-slice dose profiles, has been produced by Shope *et al.* (1982).

Effective energy and linearity of CT numbers. These data are listed in Table III. Systems using the same kilovoltage setting for brain and body scanning were studied in the brain mode only. With kilovoltages ranging from 100 to 140 kV, effective photon energies were in the interval 66–75 keV for brain and 70–79 keV for body scanning. Most systems exhibited excellent linearity of CT numbers versus μ-values over ± 50 Hounsfield Units, with correlation coefficients generally better than 0.999.

The mean values and standard deviations for all the measured data are given in Table IV for noise, uniformity of CT numbers, low-contrast detectability, spatial resolution, MTF and dose to the patient.

Discussion

This study has provided a large quantity of data on the performance of a diverse range of CT machines, much of which should be directly applicable to their use in clinical practice. No attempt has been made in this present analysis to correlate the results with such machine characteristics as scanning motion or slice thickness. The concise presentation should enable users to compare carefully-measured performance data from their own machine with another of the same type.

Similar machines from two manufacturers have given consistent results for individual parameters. An earlier survey of groups of EMI brain and body machines (Speller *et al.*, 1981) has confirmed that, except perhaps for MTF and dose to the patient, only small machine-to-machine variations for many other parameters can be expected for machines in clinical use. Consequently, it seems reasonable to assume that results obtained from a single example of a given model are representative of that model, as long as it is not seriously maladjusted. No serious maladjustments were noted with any of the single examples of CT machines considered in this study. Extreme care must be exercised with any intercomparison of different types of scanners often functioning under dissimilar operating conditions.

Slice thicknesses quoted by manufacturers are often used as the slice increment distances in multiple-slice examinations. Under these circumstances the increment should equal the Full-Width-Half-Maximum (FWHM) thickness, if clinical information is not to be missed or unnecessary radiation given to the patient. The nominal slice thicknesses quoted in this study were as specified by the manufacturers. Differences between these nominal values and the measured data are probably due to the different methods of assessment being employed. It was not always clear exactly how manufacturers assessed slice thickness, although it appears that simple beam geometry considerations were sometimes employed.

The results indicated that, for brain scanning, CT machines are now capable of providing images having noise values below 0.5% for maximum surface doses below 30 mGy, with corresponding low-contrast detectability of 2 mm and spatial resolution better than 1.5 mm. For body scanning, noise values less than 1% are attainable with marginally lower maximum doses of below 20 mGy, detectability below 4 mm and resolution better than 1.75 mm.

ACKNOWLEDGMENTS

The authors wish to acknowledge with gratitude the financial support given by Radiation Measurements Incorporated, Bureau of Radiological Health, EMI (Medical) Ltd. and Philips Medical Systems Incorporated. Mr. R. Veerappan, Mr. A. J. Coleman and Miss P. E. Waller are thanked for their help with some of the measurements. The study would not have been possible without the kind assistance and advice given by the staff at the many sites visited—we wish to thank all these colleagues most sincerely.

REFERENCES

HOUNSFIELD, G. N., 1973. Computerized transverse axial scanning (tomography) Part 1. Description of system. *British Journal of Radiology, 46,* 1016–1022.

JUDY, P., 1976. The line spread function and modulation transfer function of a computed tomographic scanner. *Medical Physics, 4,* 233–236.

SHOPE, T. B., MORGAN, T. J., SHOWALTER, C. K., PENTLOW, K. S., ROTHENBERG, L. N., WHITE, D. R. and SPELLER, R. D., 1982. Radiation dosimetry survey of computed tomography: systems from ten manufacturers. *British Journal of Radiology, 55,* (in press).

SPELLER, R. D., WHITE, D. R., VEERAPPAN, R., COLEMAN, A. J. and WALLER, P., 1981. A survey of 29 EMI CT machines in Britain. *British Journal of Radiology, 54,* 232–240.

WHITE, D. R. and SPELLER, R. D., 1980. The measurement of effective photon energy and 'linearity' in computerized tomography. *British Journal of Radiology, 53,* 5–11.

WHITE, D. R., SPELLER, R. D. and TAYLOR P. M., 1981. Evaluating performance characteristics in computerized tomography. *British Journal of Radiology, 54,* 221–231.

Book review

Computed Tomography and Cerebral Infarctions. By J. Valk, pp. 190, 1980 (Raven Press, New York).
ISBN 0-89004-646-8

It may be a surprise that a book of almost 200 pages should have been written on this subject. Yet Gardeur and Metzger produced a 300 page book on intracranial tumours as long ago as 1978, and cerebrovascular disease is much less uncommon.

Given that there is a place for a comprehensive book on the topic, is this it? Dr. Valk has produced a work based almost entirely on his own experience, which is commendable, but with the result that the factual data are spread rather thin. Indeed, only pp. 47–143 and 150–151 concern the prime subject of the book, the early pages being a technical introduction to CT and the latter sections concerned with other types of cerebral lesion. The publishers have not served the author ideally: some of the illustrations are inadequate, and the lack of inset paragraphs renders the text unattractive and at times confusing. The numerous diagrams are, however, excellent.

Dr. Valk is known as an advocate of improved international communication at congresses. It is sad to have to report that the English here is far from idiomatic: "If surgery is on the CT scan evidence no longer considered as an alternative treatment, angiography can be omitted; it serves no purpose, certainly not the interest of the patient", while unambiguous, is inelegant. Vacillation over American and British (and even Swedish) usage must be debited to the editor. There is no index.

There are factual errors or confusions: "pixel" is commonly used to mean either "picture element", in which case its dimensions are those of the image or "surface area in the patient represented by a picture element", when its dimensions correspond to real measurements in the patient. To define it simply as a "picture element" and then refer to the latter dimensions is misleading. Restriction of the term "enhancement" to only the extravascular component producing an increase in attenuation coefficients is without precedent. The passage on "hyperperfusion" compounds the widespread confusion between radionuclide, angiographic and CT findings, one of the things one would look to a book like this to clarify.

The other major point which is not resolved is the relationship of CT findings to prognosis; the author states that it is "under study in our department". He should perhaps have awaited the conclusion of that study; it is a crucial question, since it could be argued that the only role for CT in stroke is to confirm the diagnosis and exclude haemorrhage, and that unless it can give prognostic information, its contribution is entirely academic. But the author concludes: "It would not surprise me if the clinical evaluation and the response of the patient's symptoms to treatment were a far better guide to predict the outcome of a cerebral infarction than analysis of CT scan images". Work such as that of Caillé and his colleagues in Bordeaux on CT follow-up of anti-oedema therapy and its effects on prognosis is not mentioned. Unfortunately, other recent studies indicate that administration of contrast medium may worsen the prognosis in cases of cerebral ischaemia; if the almost routine high-dosage contrast regime proposed by the author were to become widely adopted, the results could be costly in more ways than one.

It will be clear from the foregoing that the question posed in the second paragraph cannot, regrettably, be given a positive answer.

I. MOSELEY.

1981, *British Journal of Radiology*, 54, 1062–1067

A simplified method of quantitating organ uptake using a gamma camera

By M. J. Myers, Ph.D., A.R.C.S., J. P. Lavender, M.B., Ch.B., F.R.C.P.(Ed.), F.R.C.R.,
J. B. de Oliveira, M.D., M.Sc. and A. Maseri, M.D., F.R.C.P., F.A.C.C.

Departments of Medical Physics and Diagnostic Radiology, Hammersmith Hospital and
Royal Postgraduate Medical School, London W12 0HS

(Received April 1981 and in revised form August 1981)

ABSTRACT

A simplified method of absolute quantitation of activity in any region of the body is presented utilizing a series of views acquired with a scintillation camera linked to a computer. An accuracy of ±6% may be achieved. No additional programming needs to be added to the standard nuclear medicine computer software and a knowledge of the attenuation coefficients involved and the shape or position of the organs examined is not presupposed or estimated. Attenuation correction is performed using a transmission image as one of the sequence of camera views. The phantom measurements used to evaluate the technique are decsribed and some clinical results presented.

So-called quantitation applied to nuclear medicine images is usually in the form of count ratios from one region to another. The usefulness of these ratios is limited since they suffer from the effects of tissue attenuation and variations in instrumental response with depth and size of the region. True quantitation of activity would, however, give added information in various clinical circumstances, particularly in such studies as ^{131}I uptake of functional thyroid metastases, in bone scans where there may be generalized changes of tracer uptake which may go undetected, in colloid scans where the distribution of functional reticulo-endothelial cells varies with diseased states, and in radiation dosimetry measurements. In our department we have previously used a twin-headed scanner for quantitation of splenic function (Szur *et al.*, 1968), uptake of tumour localizing agents (Lavender *et al.*, 1973b), bone scanning (Lavender *et al.*, 1973a) and the distribution of ^{111}I-labelled white cells (Thakur *et* al., 1977). Methods based on the gamma camera obviously have a wider application in most departments of nuclear medicine. The choice of a camera rather than a scanner for this study has been made on the basis of the wider availability of a camera interfaced to a computer and to the special properties of the parallel-hole collimator, which does not require the depth correction factors associated with the focusing collimator of a scanner.

THEORETICAL CONSIDERATIONS

A number of methods of achieving quantitation with a gamma camera/computer system have been described (Thomas *et al.*, 1976; Cauwe and Ferrant, 1979; Fleming, 1979) and are compared in Table I. We considered these to be rather elaborate, and a simpler approach requiring no new programming of the standard nuclear medicine computer system was therefore devised and tested.

All the methods are based on combining counts from anterior and posterior images of the body with correction for attenuation and radionuclide distribution to form an equation of the type

$$A = F.(N_a.N_p)^{\frac{1}{2}}.e^{-\mu L/2}.(\mu l/2)/(\sinh \mu l/2) \quad . \quad (1)$$

where A = activity in a particular region in μCi; F = instrumental calibration factor; N_a, N_p are the regional counts in an image acquired anteriorly and

TABLE I

COMPARISON OF METHODS USED TO CORRECT QUANTITATIVE MEASUREMENTS OF ACTIVITY FOR EFFECTS OF ATTENUATION AND ORGAN GEOMETRY. (SEE TEXT FOR REFERENCES AND EXPLANATION OF SYMBOLS)

Authors	Images acquired	$e^{-\mu L}$ term	$\frac{\mu l/2}{\sinh \mu l/2}$ term	Notes
Graham and Neil	A, P, Transmission, Flood	measured	—	Transmission/Flood same energy Mean of arithmetic/geometric means
Thomas *et al.*	A, P	μ calc.	μ calc.	
Cauwe and Ferrant	A, P, Lateral	μ calc. L measured	μ calc.	
Fleming	A, P, R Lat, L Lat	μ calc. L measured	μ calc. l from lateral	
This work	A, P, Transmission, Flood	measured	—	Transmission/Flood different energy

posteriorly; L, l are the body and organ thickness in the region considered and μ is the (assumed constant) linear attenuation coefficient in the projected region.

Since, in practice, it is difficult to determine the correction terms $e^{-\mu L/2}$ and $(\mu l/2)/(\sinh \mu l/2)$ without significant error due either to assumptions in developing equation (1) or to measurement of the parameters μL and l it is worthwhile to consider whether they can be more readily estimated or even omitted.

Three difficulties in accurately evaluating equation (1) are apparent. The first is estimating the attenuation term $e^{-\mu L/2}$ when the values of μ and L vary throughout the image. Each pixel in the image represents the sum effects of activity distributed in depth and attenuated by a range of material (lung, bone, liver tissue, etc.) with different attenuation coefficients. The second difficulty is estimating the term $(\mu l/2)/(\sinh \mu l/2)$ if the three dimensional shape of the organ relative to the body outline is unknown. The third is complying with the assumption of the equation since it is strictly true only on a pixel basis such that

$$A=\Sigma_i^n A_i=\Sigma_i^n F_i(N_{ai}.N_{pi})^{\frac{1}{2}}.e^{-\mu_i L_i/2}.(\mu_i l_i/2)/(\sinh \mu_i l_i/2).$$

Here Σ_i^n implies summing over n pixels in a region, each pixel itself the average over the direction normal to the collimator face. Since available methods of dealing with images acquired by the computer system almost always deal with pixels summed within a specified region of interest, the equivalence of the two sums $\Sigma_i^n(N_{ai}.N_{pi})^{\frac{1}{2}}$ and the available $(\Sigma_i^n N_{ai}.\Sigma_i^n N_{pi})^{\frac{1}{2}}$ was examined.

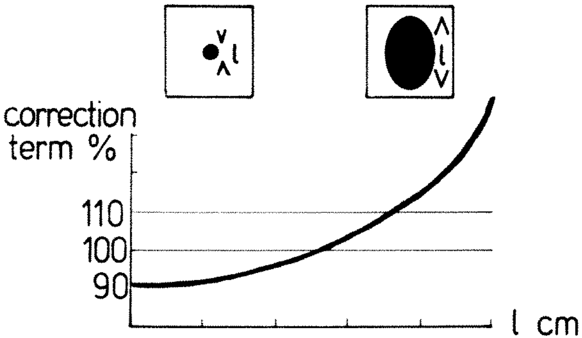


FIG. 1.

Representative correction term $(\mu l/2.100)/(\sinh \mu l/2)\%$, as a function of organ thickness l. The value of $\mu=0.12$ noted was measured with a 100 ml volume of ^{99}Tc^{m} at various depths in a 30×30×24 cm tank of water viewed by a scintillation camera.

The first difficulty may be overcome by using a transmission source to create an attenuation image. This image, needless to say, is only an approximation because of statistical limitations but has the advantage of being a locally measured one specifically for that patient. The method has been used by Graham and Neil (1974), who employed a source of the same energy as that in the emission image. In their study the transmission image had to be acquired before the radionuclide was injected into the patient, which led to a time difference between the transmission and emission study and hence to possible errors in aligning the images.

We have used a source of approximately the same energy, measured immediately after the emission source but in its own pulse height window. Because some of the emission source counts will fall within this window an emission source image is also recorded in the transmission window and is then subtracted from the previous (superimposed) image to form the final transmission image. Emission and transmission images are therefore geometrically aligned. In the common situation when the distribution of ^{99}Tc^{m} (141 keV) is to be quantitated, a readily available "flood" source of ^{57}Co (122 keV) is used for the transmission image. Despite its different energy the cobalt source was preferred to a technetium source because of its lighter construction, making it easier and safer to handle, and because of the greater differential in counts between the anterior emission and transmission images. Because the absorption coefficients for the transmission and emission sources are not the same (theoretical values in water are respectively 0.150 and 0.166 for ^{99}Tc^{m} and ^{57}Co) the single attenuation correction term used in the final calculation of activity has itself to be corrected as outlined in Appendix I.

The second difficulty, that of estimating organ size and depth, has been partially overcome by recognizing the relative invariance of the correction term as shown in Fig. 1. The term is, in effect, replaced by a single factor based on models of the organ size and patient thickness generally encountered. This approach leads to estimates to within plus or minus five to ten percent of the absolute activity. However, in those rare cases where the activity is distributed in a few isolated regions separated by a relatively large (vertical) distance such that the projected anterior and posterior images are superimposed, the absence of a correction term can lead to overestimation of up to about 20%.

The third difficulty, the difference between the sum of the individual geometric means and the geometric mean of the summed counts within the

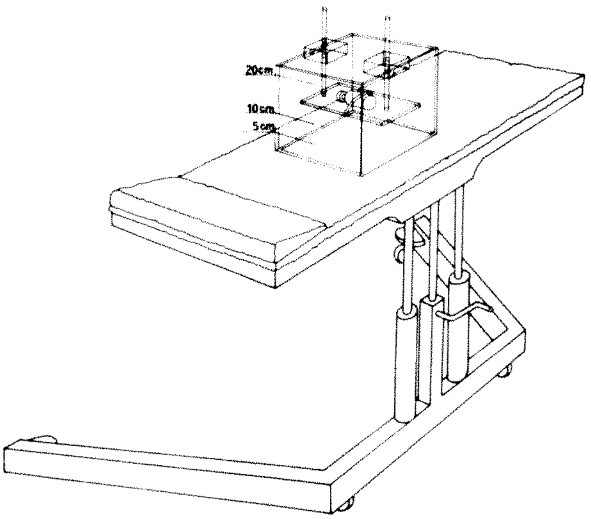


FIG. 2.

Arrangement of bottles in the water phantom used to obtain a calibration factor as a function of the source volume (68–555 ml), the position of the bottle in the tank (2–22 cm from the bottom) and the height of water in the tank (8–24 cm).

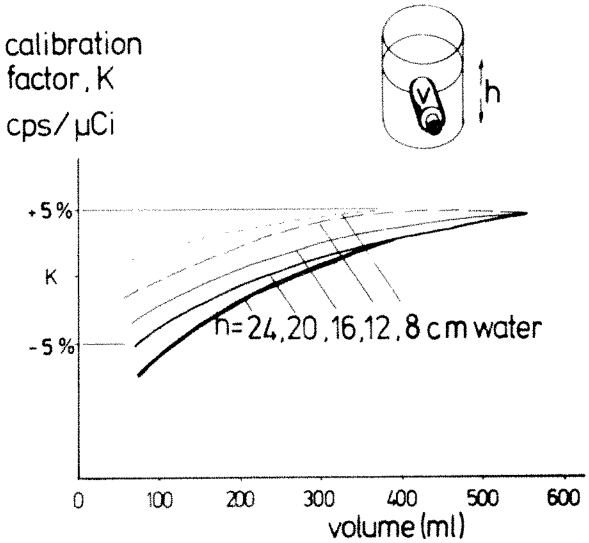


FIG. 3.

Variations of the corrected count rate obtained per μCi in the source plotted against the volume of the source. The count rate was calculated from equation (2) in the text. Curves are fitted to the count rates averaged over all measured positions of the source at a particular height of water.

region of interest, was investigated in two ways. A range of count rate distributions simulating anterior and posterior images was modelled on the computer and the difference between the two sums calculated. In addition, the calculation was performed on a range of acquired patient images. In either case the difference between the sums was of the order of a few percent and usually about 1%.

METHODS

In order to provide calibration factors and to check the accuracy of the method under a wide range of conditions, circular cylindrical plastic bottles containing measured amounts of activity were imaged in a water bath using an IGE 400T gamma camera and an MDS A^2 computer system. The arrangement is shown in Fig. 2. The parameters varied were the volume of the source (68–555 ml), the position of the centre of the source in the tank (2–12 cm from the bottom) and the total height of water in the tank (8–24 cm). For each source at each depth and amount of water anterior, posterior and transmission images were obtained. A 20% window was used and for the ^{99}Tc^{m} calibration, for example, the spectrum centred on the ^{99}Tc^{m} and ^{57}Co peaks for emission and transmission images respectively. The results are summarized in Fig. 3 and demonstrate a ±6% variation in cps/μCi over the range of parameters examined. The calibration factor found above applies only to a particular parallel hole collimator, isotope and energy setting. However, calibration factors for other conditions may be determined with fewer measurements since the first experiment demonstrates the relative invariance of the parameters examined.

The acquisition protocol adopted was as follows. After the patient was administered a previously calibrated amount of activity, positioned on the Perspex top couch and the camera face adjusted into a horizontal plane using a spirit level:

(i) an anterior view (*a*) was acquired by the computer with an energy window of 20% and at the photopeak of the emission source (*e.g.* at 140 keV for ^{99}Tc^{m}) corresponding to an absorption coefficient μ_e;

(ii) another anterior view (*b*) was acquired at the transmission source photopeak setting (*e.g.* at 120 keV for ^{57}Co) corresponding to an absorption coefficient μ_t;

(iii) without the patient having been moved or the analyser repeaked the flood source was placed on the support and a transmission image (*c*) obtained;

(iv) the camera was moved on its rails past the couch, rotated to point upwards and checked with a spirit level, moved back to the previous set position and a posterior image (*d*) obtained at the emission photo-peak setting;

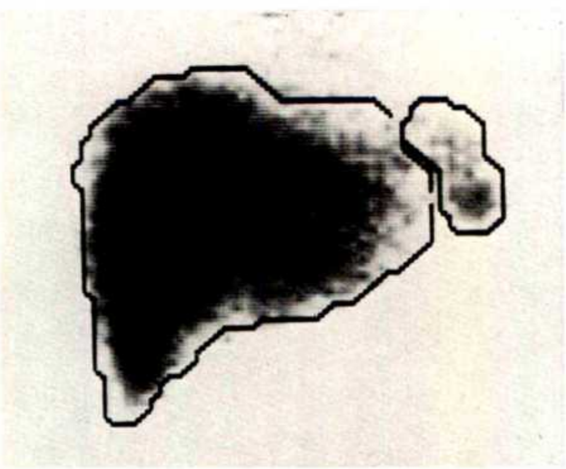


FIG. 4A.

Emission image of liver and spleen following the injection of $^{99}Tc^{m}$ in labelled sulphur colloid. Regions of interest outline the two organs.

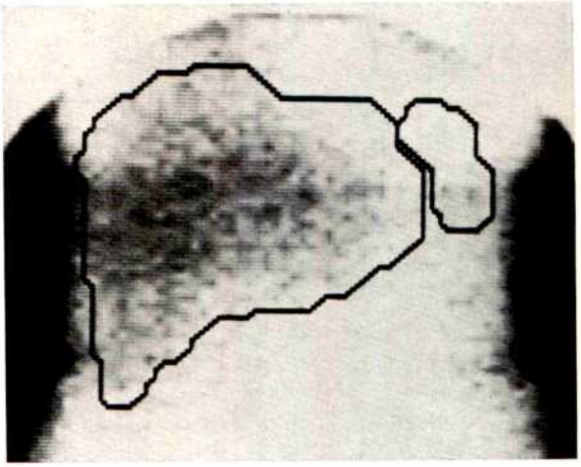


FIG. 4B.

Transmission plus emission scan of same organs using ^{57}Co disc source.

(v) at the end of the procedure a flood picture (*e*) without the patient in position was obtained by placing the disc source on the support and viewing it through the couch.

After the acquisition had been completed in the sequence described above, the computer processing of the data is carried out as follows:

(1) the images are checked for general alignment;

(2) the emission-image (*b*) is subtracted from the emission/transmission image (*c*) to obtain a bare transmission image relatively uncontaminated by spillover from the other source;

(3) an irregular region of interest is drawn on the anterior image (*a*), and transferred to the posterior image (*d*), to the difference image (*c*)–(*b*) and to the flood image (*e*). The counts within the region in each of these four images are noted as N_a, N_p, N_t, N_f respectively and the absolute activity, A, in the region calculated from

$$A = K.(N_a.N_p)^{\frac{1}{2}}.(N_t/N_f)^{\frac{1}{2}.\mu t/\mu e} \quad . . \quad . \quad (2)$$

where K is the calibration factor found as above.

If the camera/computer system allows dual isotope acquisition the method may be simplified and the procedure shortened by carrying out the steps (i) and (ii) simultaneously.

CLINICAL STUDIES

Three types of clinical study are used to illustrate this paper: a colloid liver/spleen scan (Fig. 4), a lung perfusion scan and a whole body scan following the left ventricular injection of $^{99}Tc^{m}$-labelled microspheres (Fig. 5).

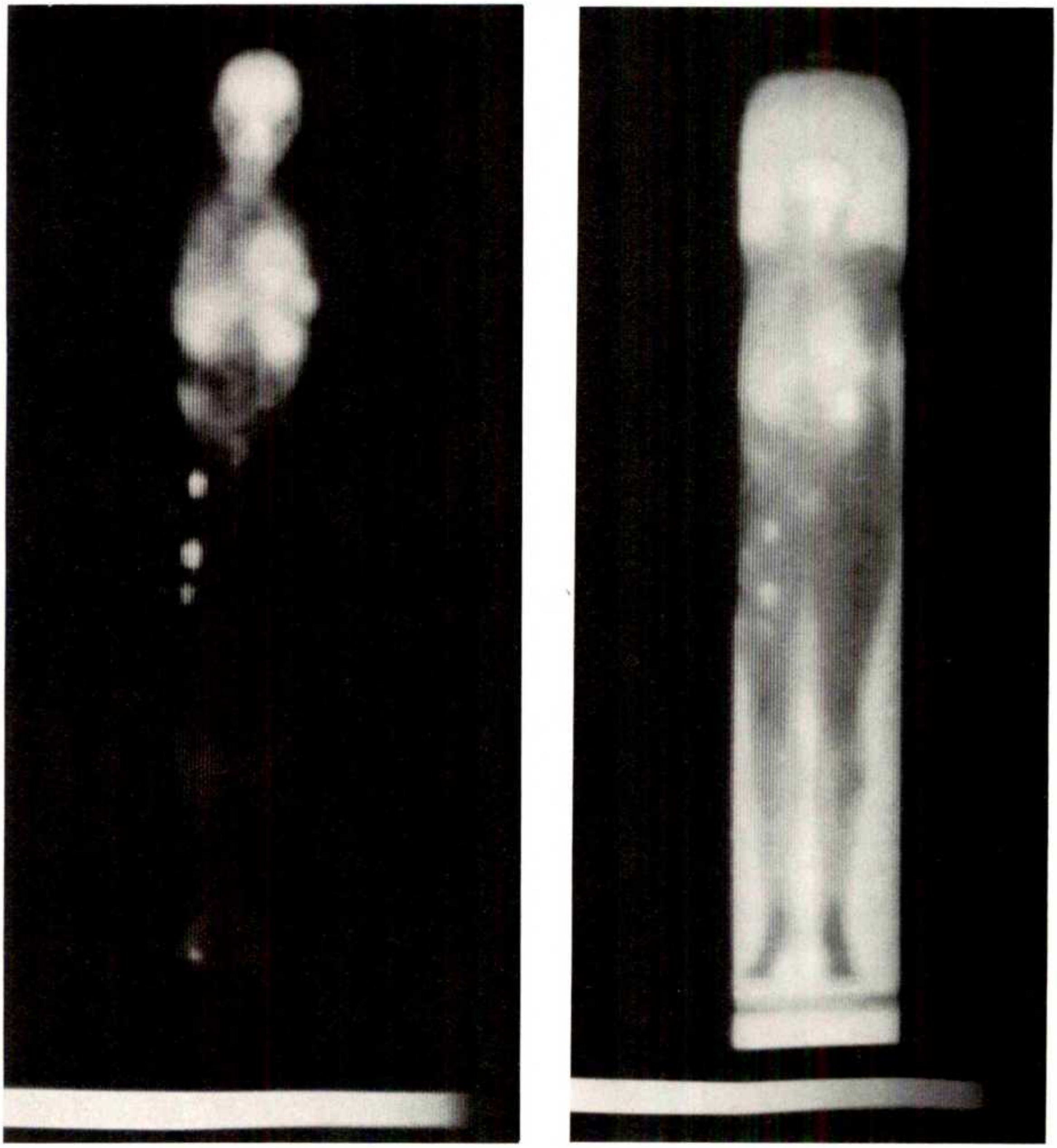
The reticulo-endothelial study of liver and spleen was performed using approximately 37 mBq (1 mCi) $^{99}Tc^{m}$-labelled sulphur colloid injected intravenously, quantitative scanning being performed 30 min after routine views had been obtained. Lung perfusion scans were also performed using 37 mBq (1 mCi) $^{99}Tc^{m}$-labelled human serum albumin macroaggregates. A quantitation was again performed approximately 30 min following the injection. The whole-body scans to show the distribution of cardiac output were performed 15–30 min after the injection of 4×10^{6} human serum albumin microspheres labelled with 370 mBq (10 mCi) $^{99}Tc^{m}$. These were injected into the left ventricular cavity during angiography.

In the case of the liver/spleen scan and lung scans the relevant organs could be contained in one view. Where whole-body scanning was required, two methods of acquiring data from patients have been used; whole-body imaging using the single-pass linear scanning facility of the camera, and acquisition of a series of individual images at four to five adjacent positions along the body.

Data showing calculated organ activity compared with injected activity on six patients is given in Table II. It can be seen that for the lungs the mean calculated retained dose in the two patients was 99% of the net injected activity. In the case of colloid scans the mean liver retention was 69% and splenic activity 7.5%. For the whole body scans total retained activity could be obtained from a summation of the sequences referred to above and showed a mean value for the five patients of 94%.

CONCLUSION

A simplified method of measuring, in quantitative terms, the uptake of activity in the whole body or individual organs using a camera/computer system has been described. Knowledge of the geometry of the distributions of radionuclide and assumptions of linear absorption coefficients are not required. Only basic region-of-interest readings are made using the computer and no extra programming is therefore involved. The method requires four, approximately



A FIG. 5. B

(A) Whole-body image showing distribution of cardiac output recorded by $^{99}Tc^{m}$-labelled microspheres injected into the left ventricle. The three areas of activity in the right leg are due to activity deposited during withdrawal of catheter.

(B) Transmission plus emission image of same patient.

TABLE II

RESULTS OF QUANTITATING ACTIVITY IN VARIOUS ORGANS

Organ (and scan finding)	Patient no.	Radiopharmaceutical	Percentage of injected activity	
Liver (normal scan)	1	^{99}Tc^{m} sulphur colloid	70% liver	7% spleen
	2		60% liver	9% spleen
	3		58% liver	7% spleen
	4		68% liver	8% spleen
Liver (enlarged liver, poor uptake)	1	^{99}Tc^{m} sulphur colloid	38% liver	19% spleen
	2		40% liver	18% spleen
Liver (area of replacement)	1	^{99}Tc^{m} sulphur colloid	51% liver	10% spleen
	2		50% liver	10% spleen
Lung (normal scan)	1	^{99}Tc^{m} MAA	95% lung	
	2		103% lung	
Whole body	1	^{99}Tc^{m} microspheres	114% whole body	
	2		96% whole body	
	3		84% whole body	
	4		79% whole body	
	5		98% whole body	

one- to two-minute, views of the patient including images acquired at the appropriate energy channel with and without a transmission source.

Phantom studies to assess the accuracy of the method for a variety of source distributions and distribution volumes indicated an accuracy of about ±6% when a general calibration factor was employed, though this might be improved for specific organs.

Representative clinical studies are presented to demonstrate that all the measured administered activity may be accounted for.

APPENDIX I

Correction for the difference in absorption coefficients for the transmission and emission sources

If $C_t = e^{-\mu_t . L}$ and $C_e = e^{-\mu_e . L}$ where C_t, C_e are the counts found in the region of interest of the image for transmission and emission source respectively having absorption coefficients μ_t, μ_e, and L is the total thickness of the body, then

$$\log C_e / \log C_t = \mu_e / \mu_t .$$

Since errors in the ratio of the two μ's are, in practice, smaller than in the values of the μ's themselves, errors in the above attenuation calculation are probably smaller than when μ alone is used in an $e^{-\mu L}$ correction term. The value of μ_e/μ_t for ^{57}Co and ^{99}Tc^{m} was measured as 1.04. The factor N_t/N_f in equation (2) was therefore raised to the power of 0.48 rather than 0.5 if a transmission source of the same energy were used.

REFERENCES

CAUWE, F. and FERRANT, A., 1979. Quantitating organ uptake with a gamma camera. *European Journal of Nuclear Medicine*, *4*, 223–229.

FLEMING, J. G., 1979. A technique for the absolute measurement of activity using a gamma camera and computer. *Physics in Medicine and Biology*, *24*, 179–180.

GRAHAM, L. G. and NEIL, R., 1974. *In vivo* quantitation of radioactivity using the Anger camera. *Radiology*, *112*, 441–442.

LAVENDER, J. P., EVANS, M. A., ARNOT, R. N., BOWRING, S., DOYLE, F. H., JOPLIN, G. F. and MACINTYRE, I., 1973a. A comparison of radiography and radioisotope scanning in the detection of Paget's disease and in the assessment of response to human calcitonin. *British Journal of Radiology*, *50*, 243–250.

LAVENDER, J. P., MERRICK, M. V. and WILLIAMS, E. D., 1973b. Application of data processing scans to measurement of the uptake and distribution of tumour localising agents (Abstract). *Journal of Physiology*, *231*,80P.

SZUR, L., GLASS, H. I., LEWIS, S. M., GRAMMATICOS, P. and DE GARRETA, A. C., 1968. Quantitative estimation of red-cell uptake in the spleen using ^{81}Rb- and ^{51}Cr-labelled red cells. *British Journal of Radiology*, *41*, 819–825.

THAKUR, M. L., LAVENDER, J. P., ARNOT, R. N., SILVESTER, D. J. and SEGAL, A. W., 1977. Indium-111-labelled autologous leukocytes in man. *Journal of Nuclear Medicine*, 18, *18*, 1014–1021.

THOMAS, S. R., MASON, N. R. and KEREIAKES, J. G., 1976. *In vivo* quantitation of lesion radioactivity using external counting methods. *Medical Physics*, *3*, 253–255.

1981, *British Journal of Radiology*, *54*, 1068–1074

Conformation therapy at the Royal Free Hospital. A progress report on the tracking cobalt project

By J. A. Brace, B.Sc., Ph.D., T. J. Davy, B.Sc., M.Sc., D. B. L. Skeggs, B.M., F.R.C.R. and H. S. Williams, M.Sc., F.Inst.P.

Departments of Medical Physics and Radiotherapy and Oncology, Royal Free Hospital, London NW3 2QG

(*Received April 1981 and in revised form July 1981*)

ABSTRACT

A computer-controlled tracking cobalt unit (CCTCU) was commissioned for treating patients in January 1980. The system has proved to be reliable and acceptable in routine use for conventional and conformation therapy. The system comprises a modified TEM MS90 Mobaltron, a Hewlett-Packard System 1000 Model 30 mini-computer and user programmes. Tracking techniques are suitable for the treatment of tumours of the oesophagus, thyroid, bronchus, chains of lymph nodes or medulloblastoma. Tumours 85 cm long can be treated at the isocentre. The high dose volume may be considerably reduced when tracking techniques are used instead of conventional techniques.

The major obstacle to the routine use of conformation therapy is treatment planning. Work in progress is designed to produce a computerized planning system linking a CT scanner and the CCTCU. It is expected that the system will produce both a plan optimized in 3-D and the necessary control data in machine readable form within an hour of a patient being scanned. The present planning system is based on a Rad-8 planning system and an Alderson phantom to verify the dose distribution in 3-D. An outline of the tracking technique is given. The computer control system is described briefly, with its method of use for treating patients. Brief reference is made to work at other centres using conformation therapy.

Conformation therapy is a term used to describe radiotherapy treatments in which the high dose volume is shaped to fit the target volume in three dimensions. This very desirable aim cannot be achieved using standard radiotherapy techniques. A tumour which is extensive, irregularly shaped or awkwardly orientated in the body, when treated by conventional techniques often has to be enclosed within an irradiated volume much larger than the tumour itself. Nevertheless, the importance of minimizing the volume of tissue irradiated to tumour dose levels is well recognized. A reduction in the irradiated volume reduces integral dose, improves the protection of sensitive organs adjacent to the target volume and also permits the tumour dose to be increased to a degree which may be clinically significant. A number of formulae have been devised which attempt to relate the tolerance dose with the treated volume (Lowry, 1973; Umegaki, 1980).

A computer-controlled tracking cobalt unit (CCTCU) was commissioned for treating patients in January 1980. The unit is used for a wide variety of treatment techniques under computer control. The most important use of the machine is the performance of conformation therapy using tracking techniques. Isodose measurements made in an Alderson phantom, using TLD and film, demonstrate considerable reductions in the high dose volume when conformation techniques are used instead of conventional techniques (Davy, 1979). The machine's ability to carry out multi-fixed-field treatments automatically is an additional useful and routinely used facility. It will be readily appreciated that in many tumour sites a high degree of conformity can be achieved by relatively simple techniques which do not involve the longitudinal tracking movement. For example, if it is necessary to treat a target volume of uniform elliptical cross-section having its axis inclined to the gantry rotation axis, this can be treated by a fixed field or arcing technique in which the beam width and collimator angle are automatically adjusted with the gantry angle. Additionally, the exposure time or gantry rotation speed may be varied with gantry angle to give any required weighting.

The CCTCU is the third of a series of machines designed to carry out tracking treatments. The first unit was based on a Marconi 250 kV arc therapy unit (Green *et al.*, 1960), while the second was a TEM Mobaltron 100 adapted for control by an analogue system (Jennings, 1965; Davy *et al.*, 1975). The CCTCU is a computer-controlled unit based on a TEM MS90 Mobaltron. The design, computer control system and applications of this machine have been described previously (Davy and Brace, 1979; Davy, 1979; Brace, 1979; Brace *et al.*, 1981). although this latest machine makes use of the same cobalt machine parameters to control the dose distribution as did the analogue controlled machine, the machine control system itself is much more versatile and easier to use, and possesses many safety features. In the old machine, the programme was stored in analogue form on two plates which advanced in synchrony with the treatment couch, and the couch therefore had to progress in order to change the value of certain parameters. In the new unit, the values are changed with time, thus conferring great flexibility on the control system. This permits use of the machine under computer control for both tracking and conventional treatments. When the machine is used for conventional techniques, the patient is set up once only, and the machine proceeds automatically to treat a succession of fixed fields.

CONFORMATION THERAPY TECHNIQUES

Conventional treatments are almost invariably planned and executed in a single plane, usually a transverse body plane. This, together with the limitations imposed by beams of rectangular cross sections, makes it difficult to shape the treated volume in three dimensions. The cross-section of the treated volume is usually constant along the tumour axis unless very complicated shielding arrangements are used or the tumour is divided into a number of short contiguous volumes treated separately. The latter method is not practical because of the risk of over- or under-dosing the interface regions.

A number of techniques have been devised to obtain conformation therapy. Proimus (1960; 1963; 1980), Trump *et al.* (1961) and Takahashi (1964) have used synchronous shielding and beam shaping devices. Umegaki (1971), Perry *et al.* (1979) and Matsuda (1980) have described machines using multi-segment collimators enabling the beam cross-section to be altered continuously.

At the Royal Free Hospital, tracking techniques developed from the original ideas of Green *et al.* (1960) are in use for treating patients. This work parallels to some extent work at other centres using linear accelerators (Levene *et al.*, 1978; Chung-bin *et al.*, 1979).

PRINCIPLE OF THE TRACKING TECHNIQUE

There are two types of tracking technique, the first combining an arcing technique with a moving table technique, and the second combining a number of fixed fields with a moving table technique. In the first type, the patient is passed slowly through the plane of rotation of the radiation source while the cobalt head arcs continuously. The couch supporting the patient is moved vertically and laterally as it advances so that, in effect, the isocentre of the machine "tracks" along a predetermined path within the patient. The shape, size and orientation of the treated zone in each body section are determined by a combination of varying beam size, arcing angle and arcing speed. The position of the high dose zone within the body contour is determined by the vertical and lateral movements of the couch. The dose delivered to any point in the treated volume depends on the time during which it is within the radiation beam and is controlled by a combination of the speed and the beam size in the direction of tracking. Figure 1 shows how the various parameters control the distribution of radiation in the patient.

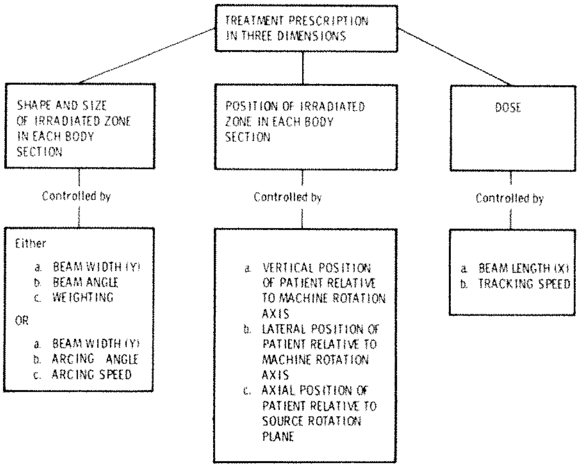

TREATMENT PRESCRIPTION IN THREE DIMENSIONS
SHAPE AND SIZE OF IRRADIATED ZONE IN EACH BODY SECTION
POSITION OF IRRADIATED ZONE IN EACH BODY SECTION
DOSE
Controlled by
Controlled by
Controlled by
Either
a. BEAM WIDTH (Y)
b. BEAM ANGLE
c. WEIGHTING
OR
a. BEAM WIDTH (Y)
b. ARCING ANGLE
c. ARCING SPEED
a. VERTICAL POSITION OF PATIENT RELATIVE TO MACHINE ROTATION AXIS
b. LATERAL POSITION OF PATIENT RELATIVE TO MACHINE ROTATION AXIS
c. AXIAL POSITION OF PATIENT RELATIVE TO SOURCE ROTATION PLANE
a. BEAM LENGTH (X)
b. TRACKING SPEED

FIG. 1.

How the various parameters control the distribution of radiation in the patient.

In the second type of treatment the patient is passed through a number of stationary beams, each beam being set to a precalculated angle of entry into the patient. The beam size may be adjusted automatically according to the tumour projection for the body section within the beam. This process is repeated for as many beams as prescribed. Treatment of the spine may only require the application of one beam.

Once the patient has been positioned on the treatment couch the whole treatment is carried out automatically under computer control as described in detail later.

THE ROYAL FREE HOSPITAL COMPUTERIZED TREATMENT SYSTEM

The treatment system comprises:

(a) a TEM Mobaltron MS90 modified for computer control;
(b) a Hewlett Packard system 1000 Model 30 minicomputer with peripherals;
(c) a suite of user programmes;
(d) a set of operating and test procedures.

The MS90 telecobalt unit operates at 90 cm source–axis distance and has a geometric field size of 45 × 45 cm at the isocentre. A pneumatically operated source wheel rotates through 95° to expose the source, the strength of which may be up to 10000 rhm. The isocentre is 126 cm above the floor which permits a 360° rotation of the head without the need for floor pits or depressions. An isocentric treatment couch similar to that used on the Ximatron treatment simulator has been adapted for use with this installation.

Two modifications have been made to the standard MS90 in order to adapt it to computer control. Firstly, drives for lateral and longitudinal couch movements were added; both the rate and position of the longitudinal motion can also be controlled. Secondly, a computer interface was incorporated. Ten parameters are under computer control, viz, shutter, collimator X, collimator Y, collimator rotation, gantry rotation, head rotation, couch height, couch lateral movement, couch longitudinal movement and floor rotation. The gantry rotation and couch longitudinal movements are controlled either to a set speed or to a set position. The range and resolution of the parameters under computer control are shown in Table I. The computer also reads the values of these ten parameters, the number of the filters inserted and the angle of rotation of the couch top about the supporting arm. At present a Hewlett Packard System 1000 Model 30 mini-computer controls the unit but any similar mini-computer could be used. However, now that the software development of the machine control programme has been completed, the mini-computer could be replaced by a micro-computer.

The CCTCU is controlled by a series of instruction groups or control vectors, each of which describes the next desired position, speed and shutter state. A computer programme reads each control vector from a disc file and translates it into a series of "words" which are then sent to the cobalt unit. Having issued the "move" instructions, the computer monitors the position and state of the cobalt unit every tenth of a second, thus checking when a set of instructions has been obeyed and also detecting any malfunction of drive which might necessitate terminating the treatment.

During commissioning, two modifications were found to be needed to achieve satisfactory control of dose levels and distribution. Firstly, since the dose is inversely proportional to the couch speed, this speed needs to be controlled very accurately. This was achieved by modifying the speed setting every second, the modification being based on the effective speed up to that point and on the distance and time remaining. Secondly, in order to achieve a sharp cut-off of dose at the beginning and end of the treatment the collimator must open and close at a rate proportional to the couch speed. This requirement was met by switching the collimator drive on and off according to the longitudinal position of the couch. Thus the collimator aperture is changed in small steps, *i.e.*, at a simulated speed.

Treatment Planning for the Tracking Technique

Since the aim is to match the high dose volume to the target volume in three dimensions, it is necessary to obtain data such as body outline, target volume and position of sensitive structures and inhomogeities, in three dimensions. Ideally this will come from a CT scanner or simulator with a tomographic facility, since both the CT images and the positional information can be obtained in a form suitable for planning purposes. For the treatment machine, the vertical and lateral displacements are specified relative to a pair of intersecting horizontal and vertical reference planes whose line of intersection runs parallel to the long axis of the patient and the gantry rotation axis. These planes are selected to coincide with the vertical and horizontal planes passing

TABLE I

The range and resolution of the therapy unit parameters which are under computer control

Parameter	Range	Resolution
Collimator X	4.0 to 44.0 cm	0.1 cm
Collimator Y	4.0 to 44.0 cm	0.1 cm
Collimator rotation	−100.0 to 100.0°	0.4°
Gantry rotation	Continuous	0.4°
Couch top longitudinal	0.0 to 85.0 cm	0.1 cm
Couch top lateral	−20.0 to 20.0 cm	0.1 cm
Couch height	−51.0 to 1.0 cm	0.1 cm
Couch floor rotation	−100.0 to 100.0°	0.4°
Head rotation	−177.0 to 177.0°	0.4°
Couch longitudinal speed	−20.0 to 20.0 cm/min	0.0784 cm/min
Gantry arm speed	−360.0 to 360.0 deg/min	1.4117 deg/min
Shutter	Open/closed	

normally through the aperture of the CT scanner or simulator. Appropriate reference lines can be marked on the patient using the scanner positioning lights. These lines are then used by the treatment radiographers to position the patient on the treatment couch. It should be noted that all displacements are specified relative to the arbitrary reference planes in the patient. The computer will automatically make any corrections necessary to allow for the actual position of the patient on the treatment couch, so it is not necessary to place the patient in exactly the same position on the treatment couch each day. In addition, an arbitrary cross-section is also selected and marked on the patient and axial displacements will always be specified from this section.

Once the patient has been scanned in the treatment position, the target volume together with any other regions of interest such as sensitive structures, is marked on as many cross-sections as required. This information is then transferred to the treatment planner, together with prescription details such as the dose required and the fractionation schedule, and, with the optimization criteria (which may be regarded as a part of the prescription), is then used by the treatment planner or dosimetrist to calculate a set of treatment machine parameters which will produce an acceptable treatment.

At present treatments are planned using a mixture of manual and computer techniques. The ten parameters under computer control can be split up into three groups, each of which has a controlling influence on a different aspect of the final dose distribution. This is illustrated in Fig.1. The value of those parameters required to produce the prescribed shape and size of the irradiated zone in each body contour can be found using a conventional treatment planning system such as a Rad-8 or an Emiplan-2. The necessary vertical and lateral couch displacements for each cross-section can also be found from the same plans, together with the tissue–air ratios which will be used to calculate the tracking speeds. Any treatment beam used must cover the tumour over the whole length of the beam and therefore the target volume entered into the planning computer should be a composite of all the sections being included within the length of the beam. (It will be appreciated that the ability of the CT scanner to provide reconstructed coronal and sagittal images is extremely convenient for this purpose).

The question of the dose calculation at any point in the treatment volume is rather more difficult since this involves the integration of the dose contributions from a large number of beams, for each of which it is necessary to know the dose profile over the whole length of the track. At present most planning systems confine the beam data to within a very short distance from the edge of the "useful" beam. Significant errors can occur during the integration if the long "tail" of the beam profile is neglected.

Optimization of the treatment plan

To deliver the prescribed dose to the tumour, a suitable combination of beam length and longitudinal couch speed must be found. The beam length is usually found first, since this depends on the tumour geometry. If the tumour is very irregular in cross-section and position in the body outline, then a short beam length will be needed to achieve a satisfactory degree of fit between the target volume and the tumour volume. This is likely to lead to protracted treatment times. If there is only a small variation in outline and position along the track, a longer beam length can be used, with a reduction in treatment time. Once the beam lengths have been chosen the tracking speeds can be calculated. In essence, an effective beam length X_e is calculated from a knowledge of the beam dose profile length. It is assumed initially that the dose received at a point P is influenced only by the TAR of the cross-section in which it is contained and not by the TAR of adjacent or distal sections. The TAR is therefore calculated for the cross-section containing P using a conventional computer planning system. The dose D_p received at point P is then given by:

$$\begin{aligned} D_p &= D_{air} \,.\, \mathrm{TAR} \,.\, t \\ &= D_{air} \,.\, \mathrm{TAR} \,.\, X_e/\tau \end{aligned}$$

where D_{air} is the in-air dose rate at the isocentre and t is the time taken for the point to pass through the beam, this being calculated from the effective beam length X_e and the tracking speed τ, *i.e.* the speed of longitudinal couch movement. In fact, the effective beam length depends to a limited extent on the thickness of the overlying tissue and allowances must be made for this.

It will be appreciated that when the appropriate treatment parameters are found using a Rad-8 planning system the dose distribution is assumed to be unaffected by what happened to the neighbouring sections. This is substantially true, but when the final assessment of the dose distribution over the whole treatment volume is taken into account, due regard must be paid to the various cross-contributions and any necessary modifications made to the treatment programme to achieve the required dose distribution. A special programme is used to integrate the dose along the locus of the isocentre.

Preparation of patient treatment control file

A special suite of programmes is used to produce a treatment file for each patient. This consists of a number of control vectors (typically 15 to 20 for a simple treatment) along with identification details of the patient, a summary of the treatment prescription, and brief details of the setting-up instructions for the radiographers. Each patient can have up to ten different treatment files to allow for changes in the treatment prescription made during the course of treatment. These treatment data are entered into the control programme by the treatment planner through a keyboard.

Verification of the treatment file

At this stage of the project it is still necessary to confirm by measurements in a phantom that the final dose distribution will be as expected. With complex treatment techniques it is essential that the dose calculations make a proper estimate of the contributions from all the beams, even though the contribution from some beams will be small and mainly due to scatter and leakage. It is also necessary to ensure that the treatment planner has correctly translated the treatment plan into the appropriate machine control data, and that these have then been accurately entered into the machine control programme through the keyboard. The phantom measurements also serve to demonstrate that the setting-up instructions are correct, and that the irradiated volume will be correctly placed within the phantom and patient. The usual procedure is first to carry out a dummy run without the phantom, to confirm that all the machine operations are as expected. The machine is observed closely throughout the test run. In addition, the computer monitors and logs all the machine operations and these are printed out for checking by the treatment planning physicist or computer scientist. Any necessary modifications or corrections are made and the programme is run again with the phantom loaded with film and TLD to measure the dose distributions. If required, runs can be carried out with the phantom in position but with the radiation shutter remaining closed.

An Alderson "Rando" phantom (Alderson *et al.*, 1962) loaded with film and TLD is used to measure the dose distributions as described by Davy *et al.* (1975). Essentially, the film gives the dose distribution while the TLD gives the dose levels. In effect the TLD is used to calibrate the film adjacent to it. It will be appreciated that the whole process, from obtaining the diagnostic and tumour localization information to producing an approved treatment programme is laborious and can take up to two weeks if performed manually.

TEST PROCEDURES

Each morning a special test programme is run by the radiographers to check that the machine is working properly. The programme tests all the machine parameters which are under computer control. Only if the test programme is satisfactorily carried out can treatments proceed.

TREATMENT PROCEDURE

The radiographer first enters the name of the patient at the computer terminal on the cobalt unit console. The full patient identification details are then displayed on the terminal and the radiographer must confirm that these are correct before the treatment can proceed. The treatment schedule is recorded in the patient's treatment file, for example, that treatment is due on that particular day. A warning will be displayed if any discrepancies are detected and the treatment will be inhibited. These warnings can only be overridden by producing a new treatment file incorporating the new requirements if it has been decided to change the total dose or the fractionation. Once it is confirmed that treatment is to proceed, the computer displays the setting-up details at the treatment console and on a monitor inside the treatment room. These details include such things as the required patient position (prone or supine), orientation with respect to the gantry, the permitted range of couch positions, and details of any filters or compensators required. The radiographer then positions the patient on the couch for treatment in exactly the same way as for other treatment machines and the computer will make any necessary corrections for the actual couch position. The CCTCU is switched from manual to computer control and the "start" button pressed. The treatment will then be carried out automatically in accordance with the control vectors in the patient's treatment file. Usually treatment will proceed without interruption until it has been completed. The unit remains under the control of the radiographer and may be halted at any time by pressing the "treatment stop" button. When this is done the computer will immediately close the shutter and stop all movements. The machine control programme is written in such a way that the radiographer can then take any of the following courses of action appropriate to the circumstances:

(1) The interrupted treatment may be resumed immediately;

(2) The radiographer can enter the treatment room to

reposition the patient and give any other attention required before resuming treatment;

(3) The treatment can be postponed and the balance of the treatment session given later;

(4) The outstanding part of the treatment session can be cancelled.

Clinical Indications for Conformation Therapy

In addition to its superiority over conventional fixed field techniques in the treatment of tumours which are irregular in shape, awkwardly orientated or tortuous, the CCTU is also able to treat long volumes, *e.g.*, medulloblastoma, at the normal SSD since the length treated is limited only by the extent of the longitudinal couch movement.

The sites for which the CCTCU is especially suitable are:

(1) Tumours in the neck such as carcinoma of the thyroid or carcinoma of the upper third of the oesophagus, where the disease plunges down into the mediastinum at a very sharp angle. In contrast to the difficulties posed by the position of the shoulders in treating these tumours by current methods, there is no problem when using the tracking technique;

(2) gynaecological tumours extending upwards from the pelvis to involve the para-aortic chain which can, using this system, be treated in continuity to a significantly increased dose, which should achieve an improvement of the present very poor results;

(3) medulloblastoma and other such tumours, which necessitate irradiation of the hind brain and the whole of the spinal axis, can be treated in less time and with greater homogeneity of dose than by any other technique now available.

In short, tumours at any site which runs a tortuous course and which can now be specifically demarcated with the aid of a CT scan are ideally suited for treatment by this system with a greatly improved prospect.

Discussion

There is a growing interest in the automation of radiotherapy machines and a number of centres have developed computer-controlled systems for supervoltage machines. The primary object of all these developments seems to be the introduction of conformation therapy. A valuable by-product is the ability to automate conventional treatments, thus permitting either an increase in the number of patients that may be treated per day or an increase in the number of fields per treatment session. Details of all treatment given on the unit are recorded by the computer.

The introduction of conformation therapy on a routine basis must await the development of computerized treatment planning systems which can optimize complex three dimensional beam configurations. As Massey (1979) pointed out, there are very few treatment planning systems in existence; most of the so-called planning systems are really dose-charting systems which rely heavily on the experience of the treatment planner. To reduce the overall time from diagnosis to the production of machine-readable control data, it is necessary to eliminate many of the time-consuming manual stages. The aim should be the automatic production of an optimized treatment plan and the corresponding machine control data. It will of course be necessary for the clinicians to outline the target volume and any sensitive structures in three dimensions and to prescribe the treatment dose and fractionation scheme, but there seems no reason why the rest of the process should not be successfully automated in the near future. It may soon be quite practical to prescribe the treatment in terms of biological effect and leave the planning system to produce the necessary plan. There are a number of conformation therapy techniques available for photon beams and it remains to be seen which system will prove the most practical in the long term.

Conclusion

The computer-controlled tracking cobalt unit has now been in routine use since January 1980. It has proved to be a reliable and acceptable system for the treatment of patients by both conventional and conformation techniques. The tracking technique is a very powerful one for controlling the shape of the treated volume in three dimensions. The major limitation on its use at present is the time required to plan and verify the treatment programme. In order to make conformation therapy available to all patients who might benefit from it, a computerized treatment planning system which can optimize dose distributions in three dimensions is required. This system must make accurate dose calculations for complex beam configurations, some of which will make only small contributions due mainly to leakage and scatter.

Work in progress at this hospital is designed to exploit the advantages of the CT scanner and the tracking technique. It is anticipated that a true treatment planning system will emerge which will link the two systems, so that the necessary machine control data will be available within an hour of the patient being scanned in the treatment position and the clinician outlining the target volume in three dimensions. It is expected that by this time a dose computation system will obviate the need for phantom measurements before treatment. The treatment techniques and planning procedures will be suitable for use with cobalt units or linear accelerators.

ACKNOWLEDGMENTS

This work has been carried out with financial support of the Department of Health and Social Security, the Imperial Cancer Research Fund and the Cancer Research Campaign. The Rad-8 planning system was generously loaned by I.G.E. (and previously by EMI Medical). The continued interest of Dr. W. A. Jennings of the National Physical Laboratory and his helpful comments on this paper are appreciated.

REFERENCES

ALDERSON, S. W., LANZL, L. H., ROLLINS, M. and SPIRA, J., 1962. An instrumented phantom system for analog computation of treatment plans. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 87,* 185–195.

BRACE, J. A., 1979. A computer system for the dynamic control of a telecobalt unit. *International Symposium on Fundamentals in Technical Progress, Liège, Belgium, May 1979* (Presses Universitaires de Liège).

BRACE, J. A., DAVY, T. J. and SKEGGS, D. B. L., 1981. A computer controlled cobalt unit for radiotherapy. *Medical & Biological Engineering and Computing, 19,* 612–616.

CHUNG-BIN, A., WACHTOR, T., ZUSAG, T. and HENDRICKSON, F., 1979. The treatment of mesothelioma of the pleura with computer controlled dynamic treatment. *Proceedings of the Fifth International Conference of Medical Physics and Twelfth International Conference of Medical and Biological Engineering, 1979* (Bellinson Medical Center, Petak Tikva, Israel).

DAVY, T. J., 1979. Dynamic treatment using a computer controlled telecobalt-60 unit. *International Symposium on Fundamentals in Technical Progress, Liège, Belgium, May 1979.* (Presses Universitaires de Liège).

DAVY, T. J. and BRACE, J. A., 1979. Dynamic 3-D treatment using a computer controlled cobalt unit. *British Journal of Radiology, 53,* 384.

DAVY, T. J., JOHNSON, P. H., REDFORD, R. and WILLIAMS, J. R., 1975. Conformation therapy using the tracking cobalt unit. *British Journal of Radiology, 48,* 122–130.

GREEN, A., JENNINGS, W. A. and CHRISTIE, H. M., 1960. Radiotherapy by tracking the spread of disease. *Transactions of the IXth International Congress of Radiology, Munich 1959,* (Urban & Schwarzenberg, Munich/Berlin), pp.766–772.

JENNINGS, W. A., 1965. Programmed 3-dimensional irradiation. *Abstracts of the XIth International Congress of Radiology, Rome 1965.* International Congress Series No. 89 (Excerpta Medica Foundation, Amsterdam), p. 332.

LEVENE, B. L., KIJEWSKI, P. K., LEE, M. C., BJARNGARD, B. E. and HELLMAN, S., 1978. Computer-controlled radiation therapy. *Radiology, 129,* 769–775.

LOWRY, W. S., 1973. The volume factor in radiotherapy. A new unit of dose: ret equivalent volume (rev). *Proceedings of the XIIIth International Congress of Radiology, Madrid, 1973.*

MASSEY, J. B., 1979. Radiotherapy treatment planning. *Postepy Fizyki Medycznej, 14,* 33–46.

MATSUDA, T., 1980. Computer controlled conformation therapy. *Proceedings of Medinfo 80 Japan,* Ed. by Lindberg /Kaihava (North-Holland Publishing Co., Amsterdam), pp. 14–17.

PERRY, H., MANTEL, J. and WEINKAM, J. J., 1979. Optimised treatment planning: automatic control of some parameters. *International Symposium on Fundamentals in Technical Progress, Liège, Belgium, May 1979* (Presses Universitaires de Liège).

PROIMUS, B. S., 1960. Synchronous field shaping in rotational megavoltage therapy. *Radiology, 74,* 753–757.

1963. New accessories for precise teletherapy with cobalt 60 units. *Radiology, 81,* 307–316.

1979. "Shell technic"; a new concept in rotational radiotherapy. *Proceedings of the Fifth International Conference on Medical Physics and the Twelfth International Conference on Medical & Biological Engineering, Jerusalem 1979* (Bellinson Medical Center, Petak Tikva, Israel).

TAKAHASHI, S., 1964. Conformation radiotherapy: rotation techniques as applied to radiography and radiotherapy of cancer. *Acta Radiologica Supplement 242.*

TRUMP, J. G., WRIGHT, K. A., SMEDAL, M. I. and SALTZMAN, F. A., 1961. Synchronous field shaping and protection in 2-million-volt rotational therapy. *Radiology, 76,* 275.

UMEGAKI, Y. 1971. The automation of radiotherapy. In *Computers in Radiotherapy: Proceedings of the Third International Conference on Computers in Radiotherapy, Glasgow 1971.* (*British Institute of Radiology Special Report Series No. 5*) pp. 147–153.

1980. Use of computers in radiotherapy—survey paper. *Proceedings of Medinfo 80, Japan.* Ed. by Lindberg/Kaihara. (North-Holland Publishing Co., Amsterdam).

Book review

Clinical Gynecologic Oncology. By Philip. J. Disaia and William T.Creasman, pp. ix+478, 1981 (C. V. Mosby Co., St. Louis; Y. B. Medical Publishers, London), £23·50. ISBN 0-8016-1314-0

The authors of this book set out to write ". . . a readable text on gynecologic oncology and related subjects addressed primarily to the community physician, resident and student involved with gynecologic patients". In fact, they have succeeded in writing a very readable and comprehensive textbook which contains so much highly specialized information that it will be of most interest to radiotherapists and gynaecologists in training. Because of the authors' clarity of style it can also be recommended to medical students and doctors with a more general interest, with the proviso that it contains more than they need to know.

The main thrust of the book concerned with the clinical aspects of tumours of the female genital tract, is excellent. Current controversies concerning management are covered without bias, and although the authors do give their preferred method of treatment the reader is left well informed and in a position to make his own decisions which can be changed later in the light of future research.

There is a good chapter on cancer in pregnancy which discusses breast cancer, leukaemia, Hodgkin's disease, melanoma and bone tumours. The weakest chapter is on tumours of the breast and here the authors lose their clear authority, especially when writing about the treatment of breast cancer. The role of radiotherapy, for instance, is barely touched upon, although the value of adjuvant chemotherapy for early breast cancer is discussed, the importance of involving these patients in clinical trials is not mentioned. The book would be better without this chapter.

In summary, this is a well written, well illustrated and well produced textbook. It is easy to read and easy to understand and a useful book of reference on the clinical aspects of gynaecological cancer.

THELMA D. BATES.

1981, *British Journal of Radiology*, *54*, 1075–1080 DECEMBER 1981

Long-term effects of pulmonary damage in mice on lung weight, compliance, hydroxyproline content and formation of metastases

By N. B. Dubravsky, B.Sc., M.Sc., Ph.D., ‡C. Dubrawsky, M.D., *S. Jampolis, M.D., †K. Mason, B.Sc., M.Sc., N. Hunter, B.Sc., M.Sc. and †H. R. Withers, M.D., Ph.D.

Department of Experimental Radiotherapy, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77030, USA

(*Received July 1980 and in revised form March 1981*)

ABSTRACT

The development of "metastatic" colonies of fibrosarcoma in the lungs of mice after IV injection of a single-cell suspension of tumour cells varied with time after irradiation or administration of bleomycin. Most notably, there was a late radiation-induced enhancement of colony-forming efficiency that coincided with an increase in lung weight and hydroxyproline content and a decrease in compliance. There was no radiation-induced enhancement of "spontaneous" metastases from a mammary carcinoma implanted in the thighs of the animals. The sequence of events after administration of bleomycin was similar to that after irradiation, but the duration of the treatment was different and the temporal relationship between enhanced colony-forming efficiency and changes in lung weight and hydroxyproline content was not as clear cut.

Increased formation of metastases after IV injection of tumour cells has been described after lung irradiation (Brown, 1973; Dao and Yogo, 1967; Peters, 1974; Van Den Brenk *et al.*, 1973; Withers and Milas, 1973) and after treatment with chemotherapy (Peters and Mason, 1977; Van Putten *et al.*, 1975). The effect is usually considered to be transient, although Thompson (1974) showed it existed 3½ and 9½ months after irradiation.

The purpose of our experiments was to study the changes in the efficiency of FSa colony formation in the lungs with time after irradiation or treatment with bleomycin (Adamson and Bowden, 1974; Luna *et al.*, 1972; Umezawa *et al.*, 1966) and to correlate these changes with quantifiable pulmonary sequels of the treatment.

MATERIALS AND METHODS

Mice. Three-month-old male mice, C3Hf/Bu, from our specific pathogen-free mouse colony were used in all experiments.

Irradiation. Anaesthetized (Nembutal, 60 mg/kg) mice were given a single dose of 1000 or 1200 cGy (rad) to the whole thorax using a dual source ^{137}Cs machine with a field size of 3.0 cm diameter and a dose rate of 1010 cGy/min. In additional experiments, different doses were used for dose response curves.

Bleomycin treatment. Groups of seven mice were injected with bleomycin (Blenoxane, Bristol, 15 mg/kg) subcutaneously twice weekly for seven weeks. At two week intervals, starting from the sixth week after the first injection, animals were killed and subjected to the studies described below.

Determination of lung compliance. Following IP anaesthesia with sodium pentobarbital (60 mg/kg), the animals were killed by severing the left renal artery at its origin from the abdominal aorta. A possible effect of agonal breathing on lung physiological measurements was prevented by opening the thorax to collapse the lungs. After securing a plastic endotracheal tube in a preformed tracheostomy, the whole thorax with the related internal organs (Gruenwald, 1964) was excised and hung on a device for measuring the pressure–volume (*p–v*) relationship, using the method described by Avery *et al.* (1959). Pressure–volume (*p–v*) readings were taken from the deflation limb and calculations included the dead space. Absolute values of compliance varied from group to group depending on factors such as age of the animal; accordingly, each experiment had its own control group and intercomparisons were not made between groups. When measurement of compliance was complete, the lungs were excised, the lobes separated, the bronchi removed, and the lobes blotted dry and weighed.

Estimation of hydroxyproline. Hydroxyproline content was used as a measure of collagen accumulation. The weighed lung lobes were minced and hydrolysed in 6N HCl at 110°C for 16–18 hours. One hundred milligrams of wet tissue were hydrolysed in 1 ml of 6N HCl. The hydrolysate was clarified by means of

---

*Present address: Department of Radiotherapy, St. Joseph's Hospital, 1835 Franklin, Denver, Colorado 80218.

†Present address: Section of Experimental Radiation Oncology, UCLA Los Angeles, California 90024.

‡Present address: McGregor Medical Clinic, 8100 Greenbriar Street, Houston, Texas.

Norit Decolorizing charcoal. The filtered solution was neutralized and diluted to give a final concentration of 5–10 μg hydroxyproline per ml.

The hydroxyproline content was estimated once or twice in each sample using the method of Newman and Logan (1950). For each set of analyses, a standard curve was constructed using a range of dilutions of a standard solution of pure hydroxyproline.

Assay of development of metastases. The tumour used is the fourth generation of a methylcholantrane-induced fibrosarcoma (FSa). A single-cell suspension of FSa cells was prepared as described previously (Milas *et al.*, 1974). Groups of mice which had completed their seven-week course of bleomycin (15 mg/kg per injection) or had been irradiated to the chest at various intervals beforehand received 5×10^4 FSa cells by injection into the tail vein. Fourteen days later the animals were killed, their lungs excised and fixed in Bouin's solution, and the number of metastases on the pleural surfaces counted.

Spontaneous formation of metastases in the lungs. The tumour used was the seventh-generation transplant of a tumour originally found outside the irradiated cervical area of a C_3H female which had received 2100 cGy of γ rays 26 months earlier. Histologically, the tumour is an undifferentiated mammary carcinoma designated MCa-K. Approximately 5×10^5 viable cells in 0.01 ml of medium were transplanted IM into the right hind legs of animals that had received a dose of 1200 cGy of γ rays to the chest 13, 48, 76, 110 or 143 days earlier. When the resulting tumours reached a mean diameter of 10 mm (16–20 days after inoculation), they were exposed to a dose of γ radiation (6000 cGy) sufficient to achieve almost 100% probability of control (Dubravsky *et al.*, 1978). Twenty-eight days later the animals were killed, the lungs weighed and fixed in Bouin's solution and the metastases on the pleural surfaces counted.

RESULTS

Lung weight, OH-proline, compliance, and formation of metastases after irradiation. The fluctuations in lung colony-forming efficiency as a function of the time between irradiation with 1200 cGy and the IV inoculation of 5×10^4 fibroscaroma cells is shown in Fig. 1. A second group of mice pre-irradiated with 1200 cGy to the chest was given an additional dose of 300 cGy to the chest 24 hours before the IV inoculation of FSa cells.

Also shown in Fig. 1 are the changes that develop in lung weight, hydroxyproline content, and compliance. In these experiments, 1200 cGy were given to different groups of mice at monthly intervals, and then all animals were killed on the same day. Thus, an effect on the various end points of aging was not accounted for. While there is no correlation between the early (24 hour) increase in lung colony-forming efficiency (LCFE) and lung weight, compliance, or hydroxyproline content, the second peak of LCFE at 120 days coincides with an increase in lung weight and accumulation of hydroxyproline and a decrease in compliance. At 159 days, when there is a decrease in LCFE, there is also a decrease in lung weight and an increase in compliance, but no change in the hydroxyproline content, indicating that changes in hydroxyproline content *per se* and LCFE are not necessarily correlated. It is also demonstrated that an

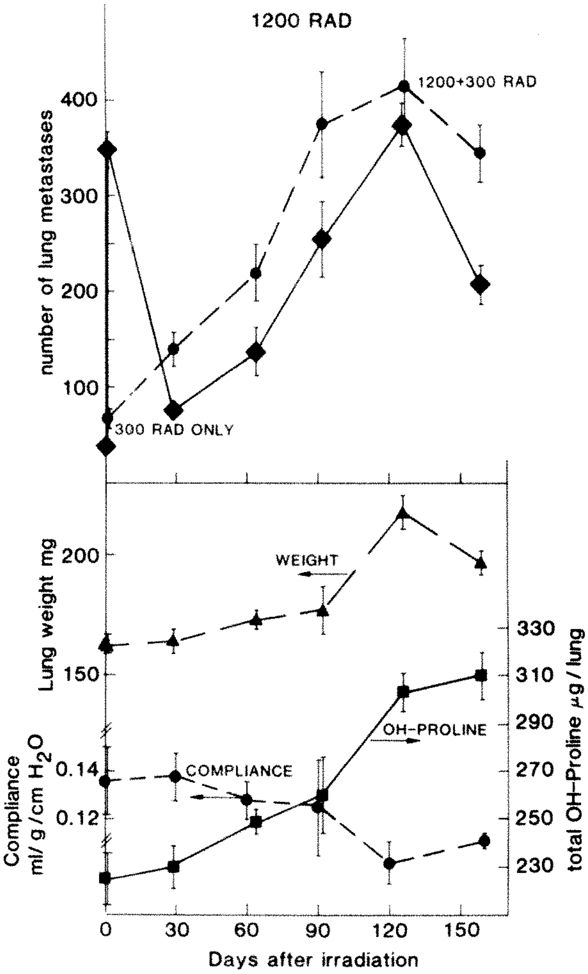


FIG. 1.

Changes in lung weight, hydroxyproline content, compliance and number of lung metastases at different times after a single dose of 1200 cGy (rad) delivered to the chest. A different group of animals was irradiated with an additional 300 cGy 24 hours before injection of FSa cells (upper section). (Bars: SEM).

additional small dose of 300 cGy caused a significant increase in the number of FSa lung metastases at all times tested. In another experiment, all mice were irradiated on the same day with 1000 cGy and groups of them, as well as controls, were killed at monthly intervals after exposure. The results of this experiment, which accounts for aging, are shown in Fig. 2. A comparison of Figs. 1 and 2 shows that although there is an increase in lung weight and hydroxyproline content with age this does not affect the conclusions to be drawn from the data shown in Fig. 1.

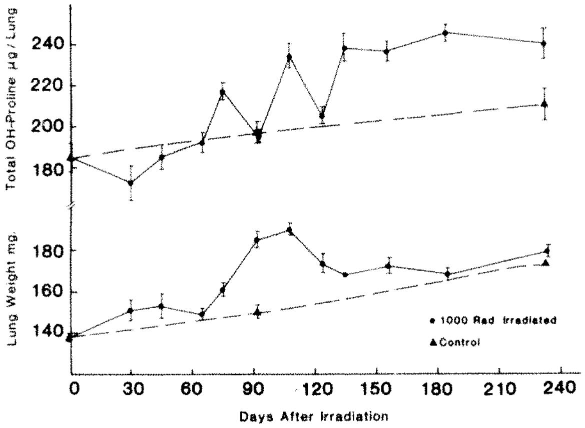


FIG. 2.

Lung weight and total hydroxyproline in the lungs of mice at different times after a single dose of 1000 cGy (rad) delivered to the chest. (Bars: SEM).

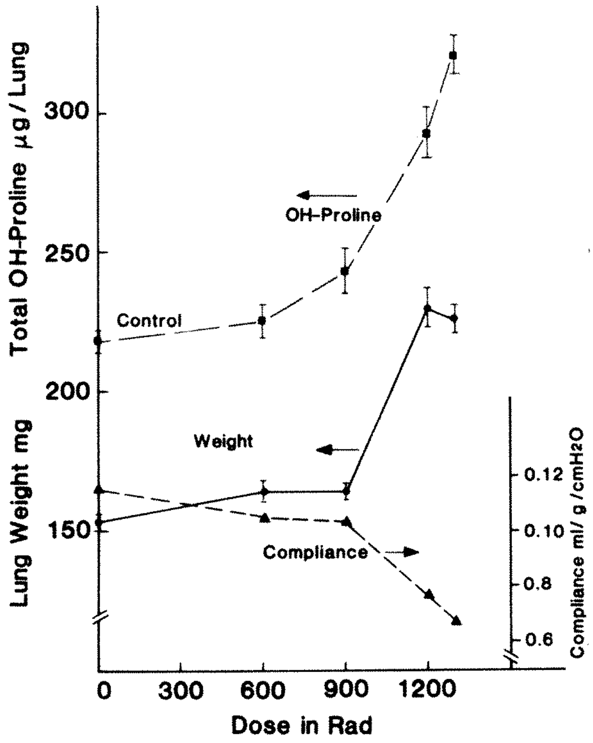


FIG. 3.

Correlation between radiation dose and lung weight, compliance and hydroxyproline content 150 days after irradiation. (Bars: SEM).

The dose-response relationship for increase in lung weights, hydroxyproline content, and compliance 150 days after irradiation is shown in Fig. 3. While there is little change in any parameter at doses less than 900 cGy, at doses of between 900 and 1300 cGy there are concomitant increases in weight and hydroxyproline content and a decrease in compliance. At higher doses, most of the animals died in less than 150 days, the LD_{50} being 1320±28 cGy (Table I).

The dose-response relationship for increase in LCFE 24 hours and 105 days after irradiation is shown in Fig. 4. The LCFE 24 hours after irradiation is increased by lower doses than is the LCFE at 105 days (200 vs. 500 cGy), but the rate of increase with increasing dose is less at 24 hours after irradiation.

The effect of bleomycin on lung weight, hydroxyproline content, compliance, and mortality. Injection of bleomycin, 15 mg/kg twice weekly for seven weeks, caused an increase in lung weight that was greatest seven days after the end of treatment (Fig. 5). The weight decreased over the next 14 days and plateaued above controls. At about 50 days it showed a second increase. At the time lung weight was maximally increased, body weight was decreased by an average of 10%. The hydroxyproline content showed a moderate early increase, but the main accumulation became evident at 49 days and showed a further increase at 63 days when the experiment was terminated. Since lung weight had decreased by this time,

TABLE I

MEAN SURVIVAL TIME (DAYS) OF CHEST-IRRADIATED ANIMALS AS A FUNCTION OF DOSE IN SINGLE EXPOSURES* (± SEM)

Dose (cGy)	Experiment no.			
	1	2	3	4
1200	134			
1300			120	130±13
1350		111±17	116±8	120±12
1400	107±15	122	103±9	114±17
1450		124± 7		125± 9
1500		111± 9	107±7	111±11
1550		122±12		116±15
1800	77± 7		103±6	

*$LD_{50/150}$ = 1320±28 cGy (rad).

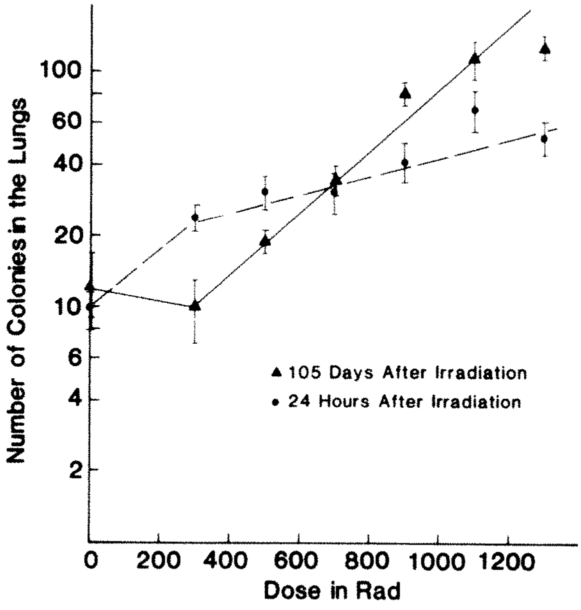


Fig. 4.

Dose-response relationship for colony forming efficiency of FSa cells in the lungs, 24 hours and 105 days after irradiation. (Bars: SEM).

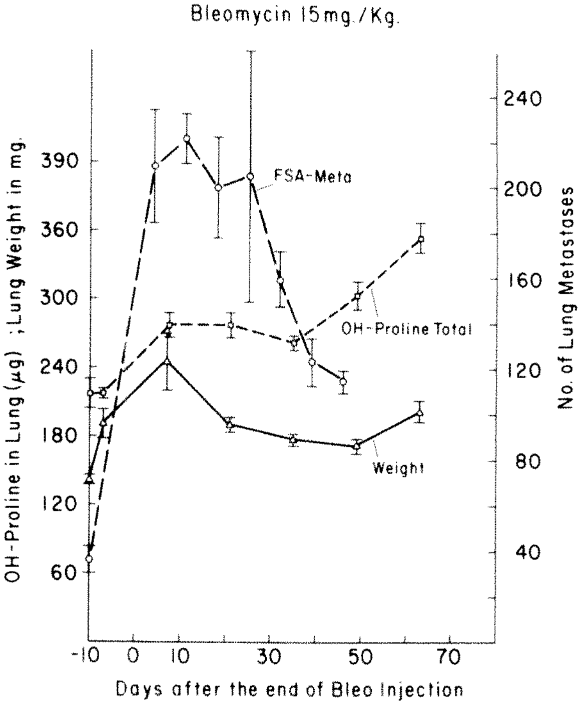


Fig. 5.

Changes in lung weight, hydroxyproline content, and the number of FSa metastases at different times after the end of treatment with bleomycin (15 mg/kg twice weekly for seven weeks). (Bars: SEM).

the increase in hydroxyproline concentration was more marked.

Lung compliance dropped significantly ($p < 0.05$) seven days after the end of treatment, from 0.114 ml/g/cm H_2O for control saline-treated animals to 0.074 mg/g/cm H_2O in bleomycin-treated animals. Recovery to just below control level followed during the next 42 days, when it almost reached control level. These changes paralleled those in lung weight. The mortality rate was about 10%, deaths occurring during the second week after the end of treatment (coinciding with the maximum acute increase in lung weight).

Development of artificial metastases in bleomycin-treated animals. The highest yield of FSa lung metastases from IV injection of 5×10^4 viable tumour cells into bleomycin-treated mice was 6.5 times greater than in control animals, and was observed during the first 25 days after the end of treatment (Fig. 5). Again, the initial increase coincided roughly with the time of increased lung weight. However, a high yield of metastases was still found 49 days after the end of treatment, by which time lung weight had decreased to about 20% above control values.

Development of spontaneous metastases from mammary carcinoma (MCa-K) at different times after irradiation. A dose of 1200 cGy was delivered to the lungs of mice at intervals of 13, 48, 76, 110 or 143 days before IM inoculation of MCa-K tumour cells into the right hind leg. Control animals with no prior irradiation of the lungs had metastases too numerous to count, and so the results are presented in terms of net metastatic tumour weight. The net metastatic tumour weight was determined by subtracting the weight of lungs from normal mice from the weight of the lungs from tumour-bearing animals. For irradiated animals, the lung weight subtracted was that of lungs of mice without tumours that had received 1200 cGy at the appropriate time before killing (Fig. 1). Figure 6 shows the weight of irradiated lung from Fig. 2 and total lung plus tumour weight of the animals with spontaneous metastases. The net weight of tumour tissue in unirradiated lungs was about 420 mg: in mice whose chests were irradiated at least 29, 64 or 92 days before tumour irradiation, the net weight of metastases in the lungs was about 200 mg. This increased to about 280 mg in animals whose lungs were irradiated 126 days before treatment of the tumour in the leg, but decreased to about 190 mg in animals irradiated 159 days before treatment of the tumour in the hind leg.

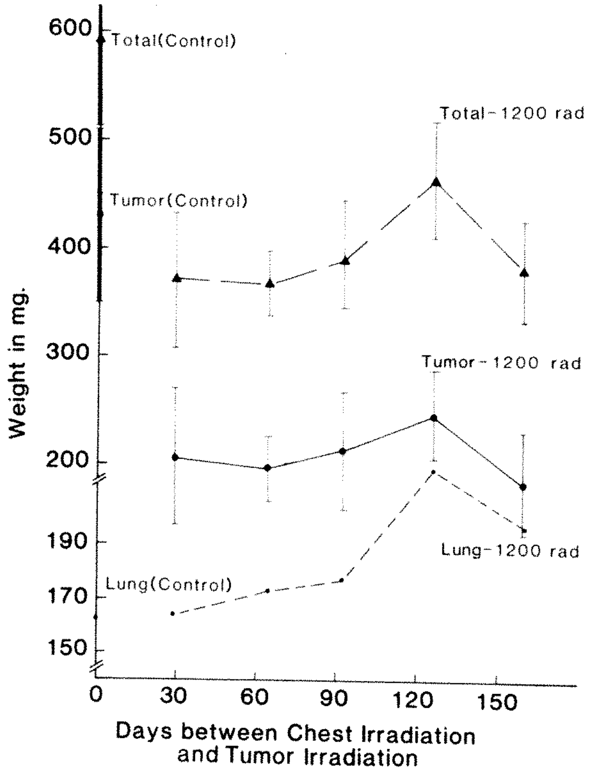


FIG. 6.

Changes in weight of lung alone, lung plus MCa-K metastases, and net weight of MCa-K metastases at different times between lung irradiation and tumour irradiation. (Bars: SEM).

DISCUSSION

Lung weight, survival, and the number of FSa lung metastases. Lung weight began to increase about 90 days after doses of 1000 cGy or more. The increase was greater and lasted longer with increased doses. In our experiments the mean survival time after doses ranging from 1200 to 1550 cGy was 103–130 days, with the majority of mice dying between 100 and 130 days after irradiation (Table I). This pattern was similar to that after X-ray or neutron irradiation of the lungs (Field and Hornsey, 1974). Field and Hornsey found the lungs of the dying animals to be highly cellular and spotted with areas of consolidation. The septal walls were thickened and alveolar space reduced. In our experiments death coincided with the time of increased lung weight in both the irradiated and the bleomycin-treated mice. This association was reported previously for rats receiving radiation to the chest (Dubrawsky *et al.*, 1975).

The late increase in lung weight in both bleomycin-treated and irradiated mice was also associated with an increase in the colony forming efficiency in the lungs of FSa cells injected IV. However, the increase in the number of FSa lung nodules in animals irradiated 24 hours before inoculation was not associated with an increase in lung weight. It is possible, therefore, that different mechanisms are involved in the early and delayed radiation-induced increases in the number of FSa lung nodules.

Hydroxyproline in the lungs after irradiation. The transient increase in lung weight about three months after doses of 1000 to 1300 cGy was followed by a sharp dose-dependent increase in total hydroxyproline in the lungs. Although lung weight decreased toward normal with time, the accumulated collagen remained. It is possible that the increase in lung weight caused a decrease in collagen concentration, which might have led to collagen synthesis. However, the increase in collagen concentration with the subsequent decrease in lung weight was not followed by a decrease in total collagen, indicating that a new equilibrium in collagen synthesis and catabolism was achieved 120 days and longer after irradiation. The reason for these changes is not clear.

Artificial and spontaneous lung metastases in pre-irradiated lungs. The increase in artificial lung metastases at short intervals after irradiation of the lungs has been described by many investigators (Brown, 1973; Peters, 1974; Van Den Brenk *et al.*, 1973; Withers and Milas, 1973) using different tumours. There is only one previous report on the effect of pulmonary damage on LCFE 3½ and 9½ months after irradiation (Thompson, 1974). In our experiments lung damage (evidenced by an increase in weight) caused by bleomycin or irradiation caused a late, transient increase in the colony-forming efficiency of FSa cells. However, an increase in LCFE was not found for spontaneous lung metastases from MCa-K mammary tumour growing in the thigh. In fact, pre-irradiation of the lungs caused a decrease in the number of spontaneous MCa-K lung metastases at all times after irradiation. This is consistent with the lack of evidence for an increase in lung metastases in patients after irradiation of the lungs (Chu *et al.*, 1967).

Radiation and bleomycin doses, experimental vs. clinical. We believe that these studies have relevance to humans treated with a single dose of irradiation to the entire lung. It was shown that the probability of developing radiation pneumonitis in humans increases from 1% at 600 cGy to 30% at 800 cGy (Fowler and Travis, 1978; Fryer *et al.*, 1978). In the mouse the same biological effect is detected after 1200 cGy to the lungs. Therefore, the basis of this research was to examine the effect of single doses of irradiation to the thorax of mice corresponding to the doses in humans causing the same biological effect.

Bleomycin was injected twice weekly for seven weeks, the total dose given being 210 mg/kg. Expression of the total dose in the mouse on a mg/m^2 basis (multiplying by 3.3) (Freireich *et al.*, 1966) results in a total dose of 693 mg/m^2. The limiting total dose for humans is 200 mg/m^2 (Gottlieb *et al.*, 1972). Here again the same biological effect is achieved by 693 mg/m^2 in the mouse as compared with 200 mg/m^2 in humans.

ACKNOWLEDGMENTS

This investigation was supported in part by grants numbered CA-11138 and CA-06294 awarded by the National Cancer Institute, DHEW. The animals used in this study were maintained in facilities approved by the American Association for Accreditation of Laboratory Animal Care, and in accordance with current regulations and standards of the United States Department of Agriculture and Department of Health, Education, and Welfare, National Institutes of Health.

We wish to thank Dr. S. P. Crook and the Bristol Laboratories, Syracuse, New York, for the supply of bleomycin (Blenoxane). We also wish to thank Dr. James H. Anderson from the department of diagnostic radiology and Dr. Melvin L. Samuels from the department of medicine for their helpful suggestions. We are grateful to Larry Wilborn and his staff for the supply and care of mice used in these experiments.

REFERENCES

Adamson, I. Y. and Bowden, D. H., 1974. The pathogenesis of bleomycin induced pulmonary fibrosis in mice. *American Journal of Pathology*, *77*, 185–198.

Avery, M. E., Frank, N. R. and Bribetz, I., 1959. The inflationary force produced by pulmonary vasculature distentions in excised lungs, and the possible relations of this force to that needed to inflate the lungs. *Journal of Clinical Investigations*, *38*, 456–464.

Brown, J. M., 1973. The effect of lung irradiation on the incidence of pulmonary metastases in mice. *British Journal of Radiology*, *46*, 613–618.

Chu, F. C. H., Lucas, J. C., Farrow, J. H. and Nickson, J. J., 1967. Does prophylactic radiation therapy given for cancer of the breast predispose to metastases? *American Journal of Roentgenology*, *99*, 987–997.

Dao, T. L. and Yogo, H., 1967. Enhancement of pulmonary metastases by X-irradiation in rats bearing mammary cancer. *Cancer*, *20*, 2020–2025.

Dubravsky, N. B., Hunter, N., Mason, K. and Withers, H. R., 1978. Dibutyryl cyclic adenosine monophosphate: Effect on radiosensitivity of tumours and normal tissues in mice. *Radiology*, *126*, 799–802.

Dubrawsky, C., Dubravsky, N. B. and Withers, H. R., 1975. Accumulation of collagen in the lungs after irradiation (Abstract). *Radiation Research*, *62*, 543.

Field, S. B., and Hornsey, S., 1974. Damage to mouse lungs with neutrons and X-rays. *European Journal of Cancer*, *10*, 621–627.

Fowler, J. F. and Travis, E. L., 1978. The radiation pneumonitis syndrome in half-body radiation therapy. *International Journal of Radiation Oncology, Biology and Physics*, 7, 1111–1113.

Freireich, E. J., Gehan, E. A., Rall, D. P., Schmidt, L. H. and Skipper, H. E., 1966. Quantitative comparison of toxicity of anticancer agents in mouse, rat, hamster, dog, monkey, and man. *Cancer Chemotherapy Reports*, *50*, 219–244.

Fryer, C. J. H., Fitzpatrick, P. J., Rider, W. D. and Poon, P., 1978. Radiation pneumonitis; experience following a large single dose of radiation. *International Journal of Radiation Oncology, Biology and Physics*, 7, 931–936.

Gottlieb, J. A. Burgess, M. A., Bodey, G. P. and Livingston, R. B., 1972. Recent developments in chemotherapy for head and neck cancer. In *Neoplasia of Head and Neck*, (17th Annual Clinical Conference on Cancer, The University of Texas System Cancer Center) (Year Book Medical Publishers, Chicago), pp. 121–133.

Gruenwald, P., 1964. Pulmonary surface forces as affected by temperature. *Archives of Pathology*, *77*, 569–574.

Luna, M. A., Bedrossian, C. W. M., Lichtiger, B. and Salem, P. A., 1972. Interstitial pneumonitis associated with bleomycin therapy. *American Journal of Clinical Pathology*, *58*, 501–510.

Milas, L., Hunter, N. and Withers, H. R., 1974. *Corynebacterium granulosum* induced protection against artificial pulmonary metastases of a syngeneic fibrosarcoma in mice. *Cancer Research*, *34*, 613–620.

Newman, R. E. and Logan, M. A., 1950. The determination of hydroxyproline. *Journal of Biological Chemistry*, *184*, 299–306.

Peters, L. J., 1974. The potentiating effect of prior irradiation of the lungs on the development of pulmonary metastases. *British Journal of Radiology*, *44*, 824–829.

Peters, L. J. and Mason, K., 1977. Enhancement of artificial lung metastases by cyclophosphamide: pharmacological and mechanistic considerations. In *Cancer Invasion and Metastasis: Biologic Mechanisms and Therapy* (Raven Press, New York), pp. 397–410.

Thompson, S. C., 1974. Tumour colony growth in the irradiated mouse lung. *British Journal of Cancer*, *30*, 337–341.

Umezawa, H., Maeda, K. and Takeuchi, T., *et al.*, 1966. New antibiotics bleomycin A and B. *Journal of Antibiotics* (*Tokyo*), *19*, 200–209.

Van Den Brenk, H. A. S., Burch, W. M., Orton, C. and Sharpington, C., 1973. Stimulation of clonogenic growth of tumour cells and metastases in the lungs by local X-radiation. *British Journal of Cancer*, *27*, 291–306.

Van Putten, L. M., Dram, L. K. J., Van Dierendouck, H. H. C., Smith, T. and Fuzy, M., 1975. Enhancement by drugs of metastatic lung nodule formation after intravenous tumour cell injection. *International Journal of Cancer*, *15*, 588–595.

Withers, H. R. and Milas, L., 1973. Influence of preirradiation of lung on development of artificial pulmonary metastases of fibrosarcoma in mice. Cancer Research, *33*, 1931–1936.

1981, *British Journal of Radiology*, *54*, 1081–1085

Turnover of proliferative cells in the spinal cord after X irradiation and its relation to time-dependent repair of radiation damage

By Shirley Hornsey, D.Sc., F.I.Biol., R. Myers, M.Sc., P. G. Coultas, Ph.D., M. A. Rogers, M.I.Biol. and Ann White, Ph.D.

MRC Cyclotron Unit, Hammersmith Hospital, London W12 0HS

(*Received April 1981 and in revised form June 1981*)

ABSTRACT

The changes in labelling index of neuroglial cells of the rat cervical cord following 20 Gy X rays are compared with the timing and pattern of the repair of radiation damage in the spinal cord. The start of time-dependent repair coincides with the release of the proliferative neuroglia from a block at the G_1/S border. The evidence suggests that the time-dependent repair reflects the normal unstimulated proliferation of the surviving neuroglial cells and that homeostatically stimulated recruitment to the proliferative neuroglia does not occur until the period just before the development of paralysis. A normal cell-cycle time of about one month for the spinal cord neuroglia is indicated from the observed pattern of labelling.

Recovery from radiation damage in the spinal cord occurs in two phases: an initial rapid phase, completed within 24 hours of irradiation, and a second much slower phase (White and Hornsey, 1978; van der Kogel, 1977a; 1979). This second phase starts about three weeks after irradiation (White and Hornsey, 1980) or later (van der Kogel, 1977b) and, although it may continue for as long as 120 days, it is largely completed within 80 days post-irradiation (Fig. 1A). The timing and pattern of this second phase of recovery is the same after irradiation with neutrons and X rays (White and Hornsey, 1980). It was previously suggested that the pattern of time-dependent repair in the spinal cord was consistent with a homeostatically triggered cell regeneration following injury (White and Hornsey, 1980). The study of labelling index at various times after irradiation reported in this paper was undertaken to test this hypothesis.

METHODS

Irradiation and labelling procedures

Full details of the irradiation procedures have been given previously (White and Hornsey, 1978). Briefly, a 1.5 cm length of the rat cervical cord (C2–C4) was irradiated with 250 kV X rays at a dose rate of 2 Gy min^{-1} using a lateral beam with HVL 1.3 mm Cu. A dose of 20 Gy was used. This dose would not cause myelopathy within the first year; it is on the upper side of doses used as the first of two equal half-doses given in the time-dependent repair study, previously reported, where the ED/50 was found to be 34.2–39.3 Gy when the doses were separated by 1–120 days (White and Hornsey, 1980).

Twenty-two three-month-old CFHB male rats (Anglia Laboratory Animals) were used in the experiment. Animals were irradiated 120, 90, 60, 45, 30, 25, 19, 16 days and one day before the start of tritiated thymidine (^{3}HTdR) injections. Two rats per treatment time were used. The ^{3}HTdR was administered to the animals in two groups, the first group consisting of rats irradiated one day to 45 days previously (4½ months old) and the second group consisting of animals irradiated 60–120 days previously (seven months old). Unirradiated rats were used as age-related controls in the two groups.

The 6-^{3}HTdR (850 GBq or 23 Ci/mMole, Radiochemical Centre, Amersham) was administered intraperitoneally every 12 h for five days. All injections contained 18.5 kBq (0.5 μCi)/g ^{3}HTdR in sterile saline.

Histological and autoradiographic procedures

Between 45 minutes and one hour after the last injection the animals were anaesthetized with ether and then killed by perfusion through the aorta with ice-cold fixative, 2% paraformaldehyde in phosphate buffer (pH 7.3). The irradiated region of vertebral column was removed from each rat and placed in ice-cold fixative, where it remained at 4°C for one week. After this time the spinal cords were dissected from the vertebral columns and embedded in paraffin wax. Transverse sections of 4 μm thickness were taken and mounted on acid-cleaned subbed slides.

Slides were coated with melted Ilford K2 nuclear emulsion diluted 50:50 with distilled water, allowed to dry and stored in light-proof boxes at 4°C for six weeks. The emulsion was then developed for five minutes in Kodak D19 developer at 14°C and fixed in Ilford's Hypan (one volume fix plus four volumes distilled water) for a further five minutes. After washing for 15 minutes, the slides were stained with haematoxylin, dehydrated, cleared in xylene and mounted in Ralmount.

Counting procedures

The white matter in transverse sections of the cord was scanned at a magnification of 1250× under oil immersion and the number of labelled neuroglial nuclei per 100 neuroglial nuclei scored. This procedure was carried out on coded slides and repeated six times within the dorsal or ventral columns of each cord, randomly selecting a different region for each count.

The neuroglial cells in the cervical cord consist of astrocytes, oligodendrocytes and microglia. The histological stains which make it possible to identify these different types of cells involve silver or gold impregnation and may interact with the development of autoradiographs. It has therefore proved impractical to attempt to distinguish the different types of neuroglial cells in the autoradiographs. Endothelial cells, nerve cell bodies and any other cell types which were obviously not glial elements were excluded from the count.

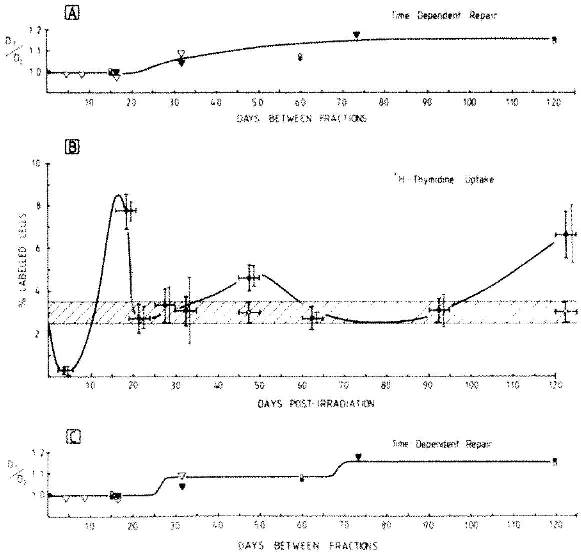


FIG. 1.

(A and C) The ratio (D_T/D_2) of the doses to cause myelopathy in 50% of rats when the dose is given in two halves separated by various times (D_T) to the dose when separated by one day (D_2) shown in relation to the time between the dose frations. The data are from White and Hornsey, 1980. ○ Cervical cord, neutrons; ● Lumbar cord, neutrons; ▽ Cervical cord, X rays; ▼ Lumbar cord, X rays. The data points in (A) and (C) are the same but different lines are drawn to join the points (see text, discussion section).

(B) The percentage of neuroglial cells in the white matter of the cervical cord labelled in five-day periods with tritiated thymidine at various times after 20 Gy X rays. Vertical bars represent standard errors based on counts from 12 regions of the cord in two animals; the thinner bar to the right joins the means of the two animals estimated separately. Horizontal bars represent the five day period over which the animals were labelled with tritiated thymidine. Open symbols are for control mice, closed symbols for irradiated mice. The hatched area represents the range of control values.

RESULTS

Figure 1B shows the mean percentages of labelled glial cell nuclei in the white matter of the cervical cord at various times after a single dose of 20 Gy of X rays. For each mean value, the relevant five day labelling period is indicated by a horizontal bar and the standard error by a vertical bar. Also shown, joined by a thin line to the right of each data point, are the percentages of labelled glial cells seen in the two individual animals concerned. Except for the 30–35 day value, the means for individual animals lie within or close to the standard errors of the means for both animals, showing that animal-to-animal variation was no greater than the field-to-field variation within the animal. Any regional variations within the cord (Hubbard and Hopewell, 1979) were not examined in this study.

Age-related unirradiated rats were labelled at the same time as the 45 day ($4\frac{1}{2}$-month-old rats) and 120 day (seven-month-old rats) post-irradiation groups. The labelling index was 2.7% ± 0.5 for $4\frac{1}{2}$-month-old and 3.7% ± 1.0 for seven-month-old rats. As these values were not significantly different, the mean value for all unirradiated rats, 3.0% ± 0.5, was used for comparative purposes in Fig. 1B.

The labelling curve shows an immediate fall with the labelling index at one to six days reduced almost to zero and significantly ($p < 0.1\%$) below the value for unirradiated cells. Labelling index during the period 16–21 days after irradiation is significantly ($p < 0.1\%$) above control levels, although the index over the 19–24 day period is within the control range. This indicates a very sharp fall in labelling index at around day 19. Labelling indices remain at about control levels until 45–50 days after irradiation when there is a suggestion that the index is slightly above control ($2\% < p < 5\%$). The index over the period 60–65 days after irradiation is indistinguishable from control values but at 120–125 days it is again significantly above control levels ($p < 0.005$).

DISCUSSION

Recovery from radiation damage in both the cervical and lumbar cord falls into two distinct phases (White and Hornsey, 1978; van der Kogel, 1977a). The initial phase occurs over the first 24 hours after irradiation and is attributed to repair of sublethal damage; the present study shows that during this time the labelling index falls abruptly. The second phase of recovery (the time-dependent repair) is slower, starting in this strain of rat sometime between 15 and 30 days after irradiation (White and Hornsey, 1980). During the time when no time-dependent repair is taking place (1–16 days) the neuroglial-cell labelling index increases 20-fold to levels significantly above control.

It has been previously suggested (White and Hornsey, 1980) that the pattern of time-dependent repair seen in the spinal cord may be due to cell regeneration, possibly stimulated by a homeostatic response to injury. Transient demyelination and Wallerian degeneration have been observed as early as two weeks after modest doses (5 Gy) of radiation (Mastaglia *et al.*, 1976) and could act as the stimulus. Such an explanation involving cell recruitment in response to early injury could account for the increased labelling index found during the 16–21 day period after irradiation in the present experiment. However, the very abrupt fall in the numbers of labelled cells at about day 19 makes such an explanation seem improbable, as the labelling index after cell recruitment would be expected to fall more gradually. A more likely explanation of the fluctuations in the labelling index found in the present study is a relatively extended cell cycle in cord neuroglia and a radiation-induced block to cell progression at the G_1/S border. We would also postulate a lack of substantial cell recruitment to proliferation until the onset of ataxia 4–12 months after irradiation. In this model the time-dependent repair observed from 20–80 days after irradiation (Fig. 1A) is more likely to be associated with the normal cell turnover of survivors and not with a stimulated cell proliferation. The following arguments support this explanation.

A radiation-induced block at the G_1/S border has been seen in several cell systems (*e.g.* Mak and Till, 1963; Coultas *et al.*, 1981). If the reduced labelling index found during the first six days after irradiation (Fig. 1B) is the result of such a block, then the overshoot from 16–21 days may be due to the release from the G_1/S block. In unirradiated animals 3% of neuroglial cells are labelled per five day interval. Thus if all blocked cells were released during the 16–21 day labelling period, a labelling index of 12% would have been expected. In fact a labelling index of about 8% was seen, but in the overlapping period 19–24 days after irradiation the labelling index was about normal and this strongly suggests that the block was partially released before the 16–21 day labelling period. The curve in Fig. 1B has therefore been drawn to take such an earlier release into account. If, as we suggest, all that has occurred is a radiation-induced block to cell progresssion at the G_1/S border, then we would also expect that the area between the curves drawn for control and irradiated animals from one to ten days after irradiation should about equal the area between these curves from 10–20 days after irradiation. The data, so far as they go, are consistent with this. From this explanation of the cell labelling pattern it follows that the start of time-dependent repair of radiation damage, sometime between 15 and 30 days after radiation, coincides with the completion of mitosis by those cells blocked for a time on the G_1/S border.

The small increase in labelling index seen over the period 45–50 days after irradiation might indicate residual synchrony amongst cells released from the G_1/S block as they enter a second S-phase. The existence of such residual synchrony would be in agreement with a cell cycle of about 30 days in cord neuroglia. It would also indicate a major difference between the proliferative pattern of neuroglia in brain and cord.

So far, the only direct determinations of cell-cycle time for neuroglia in mature animals have been made on brain, where it seems fairly well established that the cell cycle of the neuroglia is less than a day. The cells of the subependymal plate of the rat are reported to have a cycle time of 18 hours with a growth fraction of 35% (Lewis, 1968). In the mouse brain the neuroglia outside the subependymal plate have been shown to have a cycle time of 20 hours (Korr *et al.*, 1973; 1975), and a growth fraction of only 0.4% but with about a quarter of the cells leaving the growth fraction in each cycle and being replaced by recruitment from the non-proliferative glial cells.

In the absence of conflicting data it would have seemed reasonable to assume a close similarity between the neuroglial cell populations in cord and brain. However, in cord the evidence for a long cycle time, though indirect, is substantial. In addition to the suggestion of residual cell synchrony at 45–50 days after irradiation mentioned above, three further aspects of our data point towards a relatively extended cell cycle in cord. Firstly, cells with a long G_1 tend to have a long post-irradiation block at the G_1/S border compared with cells with a short cell cycle (Mak and Till, 1963; Coultas *et al.*, 1981). This may be due to a retardation of the increase in enzymes associated with DNA synthesis (*e.g.* DNA polymerases and thymidine kinase) which occur in low concentration in cells with a long G_1 and must be increased before cell progression into S can occur (Keir *et al.*, 1977). Cells with a short G_1 usually retain higher polymerase activities and are not therefore so likely to be delayed from entering S as are cells with a long G_1. Secondly, the size of the peak of labelled cells at about 15 days is readily explained on the assumption that about 3% of new cells pass through S every five days and these cells have accumulated at the G_1/S border for about 15 days. If there were only a small cohort of cells cycling about every 24 hours and producing non-proliferative but labelled daughter cells this peak would not be detectable, for only the very small cohort of stem cells would be held up. The size of the post-irradiation overshoot in labelled cells suggests that the cycle time is more than 15 days in length. Thirdly, the labelling indices at 20–30 days after irradiation are comparable with control values, suggesting that these labelled cells were in early G_1 at the time of irradiation, were not delayed at the G_1/S border and proceeded at normal rates. This would also indicate a cell-cycle time of at least 20–30 days. Additionally, Hubbard and Hopewell (1979) have found that the labelling index of neuroglial cells of rat spinal cord increased four fold as the period of continuous ^{3}HTdR labelling was extended from seven to 28 days. This observation is also consistent with a cell-cycle time of at least one month together with a low growth fraction. All these points are suggestive of a relatively long—say 15–45 days—cycle time for the proliferating neuroglia.

Figure 1A shows the time-dependent repair plotted as an isoeffect curve for radiation-induced myelopathy as a function of overall treatment time (White and Hornsey, 1980). A smooth curve has been drawn through the points from 20 to 120 days after irradiation. If the time-dependent repair is due to the proliferation of surviving cells at a relatively normal rate and that rate is based on a cycle time of approximately one month, it is tempting to draw the curve as a series of steps for the completion of each post-irradiation division. This has been done in Fig. 1C assuming that cells are going through their first post-irradiation divisions at 20–30 days. The fit suggests that the time-dependant repair is indeed associated with the increase in functional survivors in the first and second divisions after irradiation.

There is evidence that damaged or sterilized cells may divide a number of times after irradiation before dying (Silini *et al.*, 1962; Grote and Revell, 1972; Heyden and Pohlit, 1980). Cells may cease division or die after the first, second or subsequent post-irradiation divisions. Some of the sterilized cells may nevertheless be capable of normal physiological function. The loss of cells is therefore not precipitous after irradiation but builds up over the first few divisions, reaching "avalanche" proportions as damaged G_0 cells, recruited into division to replace the developing functional loss, also contribute to cell death. The rise in labelling index seen at 120 days in the present study, just before the time when animals would start showing symptoms of developing paralysis after doses slightly higher than 20 Gy X rays, may be due to this recruitment of G_0 cells into proliferation. Zeman (1963) reported a similar rise in labelling index in rat spinal cord at 140 days after irradiation. He also showed that, whereas in unirradiated animals the labelling index at three days after injection was increased from the level found three hours after injection, due to cells proceeding through mitosis, in rats with developing paraplegia the labelling index decreased over the same period and this was associated with a rise in necrotic cells. That the rise in labelling index at three to four months is due to recruitment of cells into proliferation is supported by the observations of Hubbard and Hopewell (1979) that abnormal mitotic figures seen at this time in the cervical cord were in some cases in the first post-irradiation division. If the cell proliferation cycle of about one month proposed from this study is correct, then the "avalanche" of proliferation and cell loss observed at three to four months following the second to third post-irradiation division suggests that the functional glial cells can be recruited into proliferation as demand arises.

In summary we conclude that the onset of time-dependent repair of radiation damage at 15–30 days after irradiation coincides with the recovery of the proliferative neuroglia from a block in progression to cell division. The amount of time-dependent repair in the spinal cord is small and appears to be complete by 80 days. There is no evidence of increased cell turnover nor of large-scale recruitment into the proliferative cell cohort during this period. The small extent and timing of this time-dependent repair in the spinal cord are consistent with it being due to the normal unstimulated cell turnover of surviving neuroglia. The development of symptoms which occurs from about 120 days does however coincide with a real change in cell proliferation. We postulate that this is due to the loss of functional cells from radiation death as the avalanche in recruitment to cell proliferation occurs from the glial-cells in an attempt to repair the growing cell loss.

REFERENCES

COULTAS, P. G., AHIER, R. G. and FIELD, S. B., 1981.

Effects of neutrons and X-irradiation on cell proliferation in mouse lung. *Radiation Research, 85*, 516–528

GROTE, S. J. and REVELL, S. H., 1972. Correlation of chromosome damage and colony forming ability in Syrian hamster cells in cultures irradiated in G_1. *Current Topics in Radiation Research Quarterly*, No. 7., pp. 303–309.

HEYDEN, I. R. and POHLIT, W., 1980. Proliferation of lethally damaged mammalian cells irradiated by fast electrons, fast neutrons, particles and pions. *Radiation Research, 82*, 352–363.

HUBBARD, B. M. and HOPEWELL, J. W., 1979. Changes in neuroglial cell populations of the rat spinal cord after local X irradiation. *British Journal of Radiology, 52*, 816–821.

KEIR, H. M., CRAIG, R. K. and MCLENNAN, A. G., 1977. Variation of deoxyribonucleic acid polymerases in the cell cycle. *Biochemical Society Symposium, 42*, 37–54.

KOGEL, A. J. VAN DER, 1977a. Radiation tolerance of the spinal cord: time-dose relationships. *Radiology, 122*, 505–509.

1977b. Radiation tolerance of the spinal cord: dependence on fractionation and extended overall times. In *Radiobiological Research and Radiotherapy*. IAEA-SM-212/33. (International Atomic Energy Agency, Vienna) Vol. 1, pp. 85–91.

1979. Late effects of radiation on the spinal cord. Doctoral Thesis. (Radiobiological Institute of the Organisation for Health Research TNO, Rijswijk, The Netherlands).

KORR, H., SCHULTZE, B. and MAURER, W., 1973. Autoradiographic investigations of glial proliferation in the brain of adult mice. I. The DNA synthesis phase of neuroglia and endothelial cells. *Journal of Comparative Neurology, 150*, 169–176.

1975. Autoradiographic investigations of glial proliferation in brain of adult mice. II. Cycle time and mode of proliferation of neuroglia and endothelial cells. *Journal of Comparative Neurology, 160*, 477–490.

LEWIS, P. D., 1968. A quantitative study of cell proliferation in the subependymal layer of the adult rat brain. *Experimental Neurology, 20*, 203–207.

MAK, S. and TILL, J. E., 1963. The effects of X rays on the progress of L-cells through the cell cycle. *Radiation Research, 20*, 600–618.

MASTAGLIA, F. L., MCDONALD, W. I., WATSON, J. V. and YOGENDRAN, K., 1976. Effects of X irradiation on the spinal cord: an experimental study of the morphological changes in central nerve fibres. *Brain, 99*, 101–122.

SILINI, G., HORNSEY, S. and EBERT, M., 1962. Tumour-growth and cell-viability of irradiated Ehrlich ascites carcinoma in the mouse. *International Journal of Radiation Biology, 5*, 45–47.

WHITE, A. and HORNSEY, S., 1978. Radiation damage to the rat spinal cord: the effect of single and fractionated doses of X rays. *British Journal of Radiology, 51*, 515–523.

1980. Time dependent repair of radiation damage in the rat spinal cord after X rays and neutrons. *European Journal of Cancer, 16*, 957–962.

ZEMAN, W., 1963. Disturbances of nucleic acid metabolism preceding delayed necrosis of nervous tissue. *Proceedings of the National Academy of Sciences (USA), 50*, 626–630.

Book review

Health Implications of Nuclear Power Production. Report of WHO Working Group—Brussels, 1975, pp. 75, 1978 (World Health Organization, Copenhagen), Sw. Fr. 8.
ISBN 92-9020-103-7

This publication is a report of a working group convened in 1975 by the World Health Organization (Regional Office for Europe) in collaboration with the Government of Belgium. The objective was to appraise the effects of nuclear power on man and the environment. The working group was multidisciplinary in expertise and their report covers possible health detriment associated with all phases of nuclear power generation, identifying the important ones as occupational accidents during mining and construction, exposure of uranium miners to radon and its daughters, the radiation exposures of workers in reactor installations and in fuel reprocessing facilities and the collective dose to the world population from long-lived gaseous radionuclides.

Recognizing the need to compare health effects which may result from the exploitation of nuclear energy with those associated with alternative energy sources, the report draws attention to the absence of knowledge on many aspects of non-nuclear technology and recommends the encouragement of appropriate research. Other recommendations concern only the nuclear-fuel cycle and these include the collection of epidemiological data on genetic and somatic effects of radiation, the direction of resources to permit an objective consideration of radioactive-waste management options, the provision for handling accidents involving high acute radiation doses and the review of emergency procedures to protect the public in the event of a serious accident. The report also discusses the treatment of chemical wastes, the effects associated with the discharges of heated water, acts of sabotage, training of personnel, the siting and decommissioning of nuclear plant and the importance of disseminating information as widely as possible.

In 63 pages of text, the document summarizes the entire nuclear fuel cycle from mining through fuel preparation and electricity generation to reprocessing and the handling of radioactive waste. The working group resisted the temptation to produce a 1000 page review and instead produced this useful, readable and concise statement. Although there have been a number of developments in the six years since this report was first drafted, the summary view it presents is still valid.

J. REISSLAND.

1981, *British Journal of Radiology*, *54*, 1086–1090

Thermal resistance in a spontaneous murine tumour

By *Jane Maher, M.B., M.R.C.P., M. Urano, M.D., Ph.D., L. Rice, M.S., and H. D. Suit, M.D., D.Phil.

Department of Radiation Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114, USA

(*Received May 1981*)

ABSTRACT

Resistance to subsequent hyperthermia as a result of prior heating was investigated using a spontaneous murine tumour implanted into the feet of C3H/Sed mice. Tumours were treated by immersing the tumour-bearing foot into a constant-temperature hot water bath set at 45.5°C and were given single and split doses of heat. Response was assessed using a tumour-growth time assay. Three aspects of thermally-induced resistance were particularly considered: the time course of development and decay; the importance of the magnitude of the priming dose and the influence of the size of the tumour at the time of treatment.

Substantial resistance was induced in this tumour by short priming doses at 45.5°C, rising rapidly 1–2 days after the first treatment and then starting to decay. There was no significant difference in the kinetics of thermal resistance induced in tumours treated at 4 mm and those treated at 8 mm in size, although the larger tumours were more sensitive to single doses of heat. Increasing the magnitude of the priming dose of heat resulted in an increase in the magnitude of resistance to the second dose.

The results of this study are compared with results of similar studies in this and other laboratories using murine normal tissues and cells in culture. Possible clinical implications are considered.

There has been a serious and growing interest in the use of localized hyperthermia for the treatment of patients with cancer. Moderate levels of hyperthermia lethally damage mammalian cells. The cell-survival curve for heat is very similar in shape to that for ionizing radiation. One aspect of cell killing by hyperthermia which is quite different from that for radiation is the development of "thermal resistance" or thermotolerance. Following a single heat treatment, cells *in vitro* have been shown to develop resistance to subsequent heat treatment (Gerner and Schneider, 1975). This resistance is transient and non-heritable and may be defined as an increase in D_0 of the cell-survival curve induced by prior heat treatment with or without a change in shoulder (Henle and Dethlefsen, 1978). The thermal resistance develops rapidly in several to 24 hours after initial treatment and then decays slowly. It may develop during the treatment when cells are treated at temperatures below 43°C at normal pH (Gerweck, 1977).

Recent studies have demonstrated similar resistance in murine normal tissues (Law and Field, 1979; Hume and Marigold, 1980; Urano *et al.*, 1980a; b; Rice *et al.*, 1981) and in some tumour systems (Maher *et al.*, 1980; Overgaard and Suit, 1980), although no detailed studies have been reported on the kinetics of thermal resistance in tumours. It is clearly of interest to study the thermal response of both normal tissues and tumours in search of exploitable differences in the kinetics of thermal resistance which might lead to therapeutic gain in the clinic.

In the present studies, we have investigated the kinetics of thermal resistance and the effect of the size of the priming dose on the development of resistance. Urano *et al.* (1980a) have already shown that larger tumours may be more sensitive to a single heat dose than smaller tumours. Presumably the proportion of nutritionally deprived heat-sensitive cells may increase in the larger tumours. We have therefore studied the effect of tumour size on the kinetics of thermal resistance.

MATERIALS AND METHODS

The animals used were 8–10 week old C3Hf/Sed mice from our defined-flora colony (Sedlacek and Mason, 1977). Sterilized Wayne Lab Blox and acidified vitamin-K fortified water were provided *ad libitum*. Tumours were 8th generation isotransplants of a fibrosarcoma which arose spontaneously in a C3Hf/Sed mouse and are designated as FSa-II. The tumour was extremely weakly immunogenic, and the volume doubling time over the volume range of 100–200 mm^3 was about two days.

Single-cell suspensions were prepared by a trypsinization procedure which has been reported elsewhere (Urano *et al.*, 1976). Approximately 10^5 viable tumour cells in 5 μl were transplanted into the subcutaneous tissue of the mouse foot. Hyperthermia was given by immersing the foot of the unanaesthetized animal into a water bath maintained at the desired temperature ±0.1°C (by a constant temperature circulator, Lauda type B-1, West Germany). The temperature in the central region of the tumour equilibrated within 1–2 minutes of immersion (Urano *et al.*, 1980a).

Tumour response was assessed by tumour-growth time analysis, *i.e.*, the time taken for the treated tumours to reach 1000 mm^3 from the time of the first treatment. Three diameters of each tumour (d_1, d_2 and d_3) were measured three times a week using a caliper, and the tumour volume was calculated by the formula $\pi d_1 d_2 d_3/6$. The tumour-growth time was noted for each tumour and the median was calculated for each group by logit analysis.

---

*Department of Oncology, The Middlesex Hospital Medical School, London W1P 7PN, England.

RESULTS

The kinetics of thermal resistance were studied in FSa-II tumours of two sizes heated at 45.5°C. The first dose (D_1) of 10 minutes was given when tumours reached an average diameter of 4 or 8 mm. The second dose (D_2) followed at various time intervals T_i and the tumour-growth time was studied. The upper and lower panels of Fig. 1 demonstrate this as a function of total treatment time for 4 and 8 mm tumours respectively. The dose-response curves for the split-dose treatments are markedly less steep than for the single dose. This is true for both 4 and 8 mm tumours, indicating development of substantial thermal resistance in both sizes of tumours.

To investigate the kinetics of thermal resistance the treatment time at 4.5°C required to induce a constant tumour-growth time of 20 days (T_{20}) was calculated from each dose-response curve shown in Fig. 1. This is plotted as a function of T_i in Fig. 2, where the development and the decay of thermal resistance is evidenced as an increase and decrease in the T_{20}. Notably, the thermal resistance developed rapidly in the first 1–2 days and then started to decay. Even at a T_i of five days, the T_{20} was 1.5 times longer for a single dose. This effect at five days may be attributed in part to significant regrowth of the FSa-II tumour during the five-day interval rather than to the consequence of persistent resistance alone.

There appeared to be no significant difference in the kinetics of thermal resistance between 4 and 8 mm tumours, although the 8 mm tumours were more sensitive to single treatment than the 4 mm tumours as evidenced by the different slopes of the dose-response curves for tumours of these two sizes (Fig. 1).

The effect of the magnitude of a priming dose on the induction of thermal resistance in the FSa-II tumours was also investigated. A D_1 of 3 to 22.5 minutes was given when tumours reached an

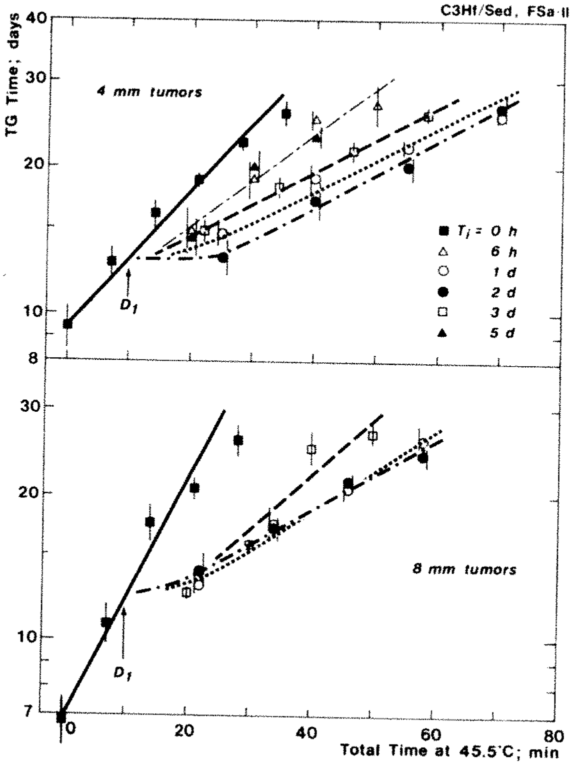


FIG. 1.

Effect of two hyperthermia treatments given at 45.5°C on tumour-growth (TG) time of FSa-II tumours. The first dose (D_1) of ten minutes was given when tumours reached an average diameter of 4 mm (upper panel) or 8 mm (lower panel). The second dose followed with a varying time interval (T_i) as indicated in the figure. Vertical bars are 95% confidence limits.

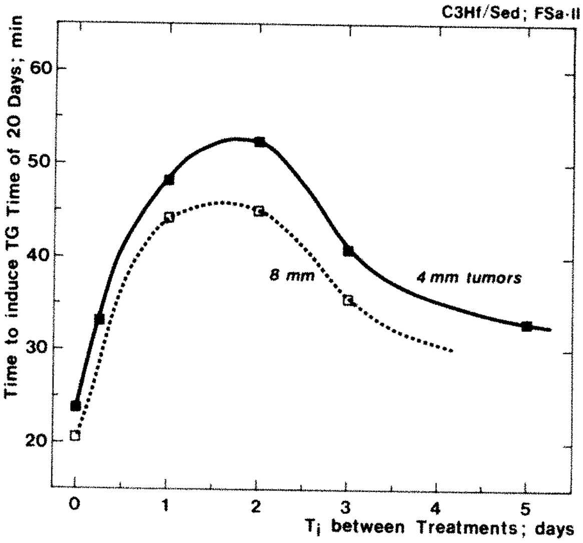


FIG. 2.

Effect of the time interval between two doses on the treatment time to induce a tumour-growth (TG) time of 20 days. The treatment time was calculated from the regression lines in Fig. 1. Solid and open symbols indicate 4 and 8 mm tumours.

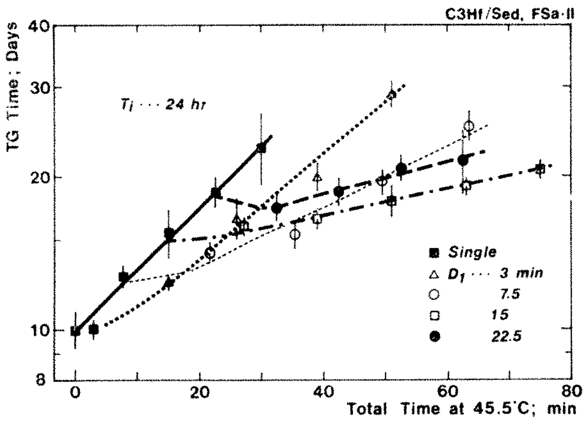


FIG. 3.

Effect of the size of first dose on thermal resistance. The first dose was given when tumours reached an average diameter of 4 mm. The second dose followed 24 hours later. Vertical bars indicate 95% confidence limits.

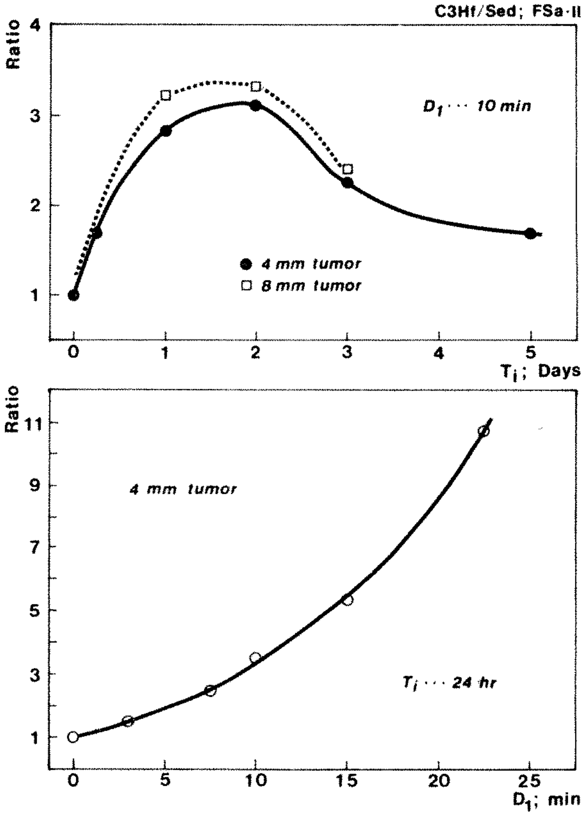


FIG. 4.

The kinetics of thermal resistance. The thermal resistance ratio was calculated according to Eqn. 1 and plotted as a function of time interval (upper panel) or of size of first dose (lower panel). The biological endpoint used to calculate the ratio is the treatment time to induce a tumour-growth time of 20 days.

average diameter of 4 mm, and was followed at 24 hours by a variable D_2. The tumour-growth time is plotted in Fig. 3 against total treatment time for each value of D_1. The dose-response curves after the second dose show a decrease in the slope with increasing D_1, although the slopes following D_1 of 15 and 22.5 minutes are comparable. These data suggest that an increasing D_1 is associated with increasing magnitude of the thermal resistance. This is more clearly evidenced in Fig. 4 where thermal resistance ratio (TRR) is plotted as a function of D_1 (lower panel). The TRR is defined as

$$\mathrm{TRR}=\frac{D\,(\text{total dose})-D_1}{D\,(\text{single dose})-D_1}\ \text{or}\ \frac{D\,(\text{second dose})}{D\,(\text{single dose})-D_1}\quad(1)$$

where D is a treatment time to induce a given biological endpoint, a tumour-growth time of 20 days. Expression of the TRR in *in-vivo* systems was also extensively discussed in our previous paper (Rice *et al.*, 1981).

DISCUSSION

The present experiments have demonstrated development of substantial thermal resistance in a murine tumour. The kinetics of thermal resistance are very similar to those found in cultured mammalian cells and in mouse normal tissues (Gerner and Schneider, 1975; Henle and Dethlefsen, 1978; Law and Field, 1979; Rice *et al.*, 1981). The upper panel of Fig. 4 demonstrates the TRR as a function of T_i between two doses where the TRR was calculated by Eqn. 1. It is obvious that substantial resistance developed within one day and then decayed slowly. Only partial decay was evident even after five days after the priming dose, although regrowth of the tumour might have contributed significantly to the increase of TRR.

Thermal resistance increased with increasing priming dose (lower panel in Fig. 4). This finding is also comparable to that observed in cultured cells and in normal mouse tissues (Gerner *et al.*, 1976; Harisiadis *et al.*, 1977; Law and Field, 1979; Rice *et al.*, 1981). This increase in resistance could result not only from an increase in D_0, but also from an increased shoulder of the dose-response curve. Therefore, the thermal resistance in tumour tissues could not be directly compared with that in normal tissues already reported by us (Rice *et al.*, 1981), because of different endpoints, *i.e.*, level of tissue damage evaluated. The endpoint in our normal-tissue studies was the treatment time to induce a loss

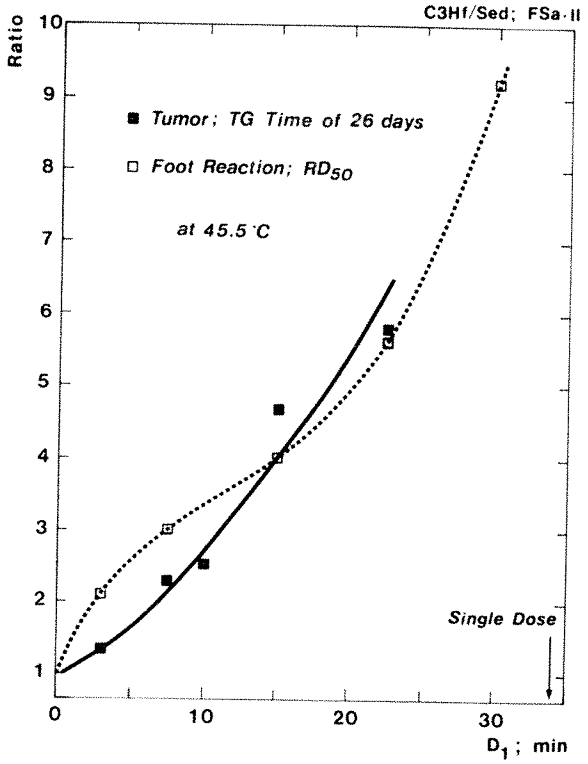


FIG. 5.

Thermal resistance ratio for FSa-II tumour and for the mouse foot. The calculation of the ratio was based on biological endpoints produced in both tissues by the same single dose. The endpoint for foot reaction was loss of at least one toe (RD_{50}) while that for tumour response was treatment time to induce a tumour-growth (TG) time of 26 days. Both endpoints were obtained by the same single dose of 34 minutes at 45.5°C. RD_{50} values are from previous experiments (Rice *et al.*, 1981).

of one toe or a greater reaction in half the treated animal feet, RD_{50}. The single-dose RD_{50} at 45.5°C was 34 min which in our FSa-II tumours induced a tumour-growth time of 26 days (T_{26}) as seen in Fig. 1. Accordingly, the RD_{50} (cited from Rice *et al.*, 1981) and T_{26} have been used as endpoints to calculate the TRR (some T_{26} values were obtained by extrapolating each dose-response curve) which is shown in Fig. 5 as a function of D_1. The T_i between D_1 and D_2 was 24 hours. There is apparently a difference in the TRR after a small D_1 as a rapid increase in the TRR appears to be a specific feature of the foot reaction. No other significant difference in the thermal resistance is seen between the murine foot and the FSa-II tumour. This might imply that only small doses result in a therapeutic gain if each dose is given when the thermal resistance has fully developed. However, it should be noticed that this is a finding in a single spontaneous tumour treated at a single representative temperature. We have further investigated thermal resistance in other spontaneous and chemically-induced tumours. Preliminary results in these studies suggest a greater thermal resistance in the spontaneous tumour than in the mouse foot.

The evidence that the magnitude of thermal resistance increases with an increasing D_1 raises a critical question as to the efficacy of differential heating, *i.e.*, a greater dose (or higher temperature) to the tumour than to the surrounding normal tissue. The tumour tissue receiving this larger dose may develop a greater thermal resistance to subsequent treatment compared with the normal tissue, thus cancelling any therapeutic gain.

It has been demonstrated in cultured mammalian cells that a decrease in microenvironmental pH is associated with an increased thermal sensitivity to single heat treatment (Gerweck, 1977; Overgaard, 1976). An animal study in our laboratory demonstrated that large tumours were more sensitive to heat than small tumours, perhaps because the tissue pH decreases with increasing tumour size (Urano *et al.*, 1980a). Recently, it has been observed that the decreased pH inhibits the development of thermal resistance (Nielsen and Overgaard, 1979; Goldin and Leeper, 1980), although Gerweck *et al.* (1980) reported that thermal sensitivity at low pH was more pronounced in cells exposed to single treatments of hyperthermia than to fractionated treatments. The present experiments, however, apparently failed to demonstrate a significant difference in the kinetics of thermal resistance between 4 and 8 mm tumours. The possible causes of this failure might be that the pH in 8 mm tumours was not sufficiently low to inhibit the development of thermal resistance as compared to the pH in 4 mm tumours, or that the first treatment reduced the tissue pH in tumours of both sizes to a comparable level.

We have demonstrated development of substantial thermal resistance in a spontaneous murine tumour. Only little is yet known about the kinetics and the mechanism of thermal resistance. Obviously, however, the thermal resistance may be a critical factor in determining the success of certain protocols of clinical hyperthermia. particularly those featuring multiple treatments (LeVeen *et al.*, 1980; Storm *et al.*, 1980). Further investigations are needed to elucidate the dependence of resistance on the temperature level used in the initial or subsequent treatments, the role of histological type of the tumour, and the importance of thermal resistance if the treatment is given in multiple fractions.

ACKNOWLEDGMENTS

This investigation was supported by CA Grant Numbers 26350 and 13311 awarded by the National Cancer Institute Department of Health, Education and Welfare.

Support for Jane Maher provided by Cancer Research Campaign and King Edward's Fund, London.

REFERENCES

Gerner, E. W., Boone, R., Connor, W. G., Hicks, J. A. and Boone, M. L. M., 1976. A transient thermotolerant survival response produced by a single thermal dose in HeLa cells. *Cancer Research*, *36*, 1035–1040.

Gerner, E. W. and Schneider, M. J., 1975. Induced thermal resistance in HeLa cells. *Nature*, *256*, 500–502.

Gerweck, L. E., 1977. Modification of cell lethality at elevated temperatures. The pH effect. *Radiation Research*, *70*, 224–235.

Gerweck, L. E., Jennings, M. and Richards, B., 1980. Influence of pH on the response of cells to single and split doses of hyperthermia. *Cancer Research*, *40*, 4019–4024.

Goldin, E. M. and Leeper, D., 1980. The effect of low pH on thermotolerance induction (abstract). *Radiation Research*, *83*, 431.

Harisiadis, L., Sung, D. and Hall E. J., 1977. Thermal tolerance and repair of thermal damage by cultured cells. *Radiology*, *123*, 505–509.

Henle, K. J. and Dethlefsen, L. A., 1978. Heat fractionation and thermotolerance: a review. *Cancer Research*, *38*, 1843–1851.

Hume, S. P. and Marigold, J. C. L., 1980. Transient, heat-induced thermal resistance in the small intestine of mouse. *Radiation Research*, *82*, 526–536.

Law, M. P. and Field, S. B., 1979. Induced thermal resistance in the mouse ear. *British Journal of Radiology*, *52*, 308–314.

LeVeen, 1980. Radio-frequency therapy: clinical experience. In *Thermal Characteristics of Tumors: Applications in Detection and Treatment*, *Vol. 335*. Eds. Rakesh K. Jain and Pietro M. Gullino (New York Academy of Sciences), pp. 362–371.

Maher, E. J., Urano, M., Rice, L. and Suit, H. D., 1980. Kinetic studies of thermal resistance in spontaneous murine tumours (Abstract). *Radiation Research*, *83*, 459.

Neilsen, O. S. and Overgaard, J., 1979. Effect of extracellular pH on thermotolerance and recovery of hyperthermic damage *in vitro*. *Cancer Research*, *39*, 2772–2778.

Overgaard, J., 1976. Influence of extracellular pH on the viability and morphology of tumour cells exposed to hyperthermia. *Journal of the National Cancer Institute*, *56*, 1243–1250.

Overgaard, J. and Suit, H. D., 1980. Multifractionated hyperthermia treatment of malignant and normal tissue *in vivo*. *Cancer Research*, *40*, 2045–2050.

Rice, L., Urano, M. and Maher, E. J., 1981. The kinetics of thermotolerance in the mouse foot. *Radiation Research* (in press).

Sedlacek, R. S. and Mason, K. A., 1977. A simple and inexpensive method for maintaining a defined flora mouse colony. Pt I. *Laboratory Animal Science*, *27*, 667–670.

Storm, F. K., Morton, D. L., Kaiser, L., Harrison, W. H., Elliott, R. S., Weisenberger, T., Parker, R. G. and Haskell, C. M., 1980. Clinical local hyperthermia by radio frequency: a review. *Third International Symposium, Cancer Therapy by Hyperthermia, Drugs and Radiation*, June 22–26, 1980.

Urano, M., Gerweck, L. E., Epstein, R., Cunningham, M. and Suit, H. D., 1980a. Response of a spontaneous murine tumour to hyperthermia: factors which modify the thermal response *in vivo*. *Radiation Research*, *83*, 312–322.

Urano, M., Nesumi, N., Ando, K., Koike, S. and Ohnuma, N., 1976. Repair of potentially lethal radiation damage in acute and chronically hypoxic tumor cells *in vivo*. *Radiology*, *118*, 447–451.

Urano, M., Rice, L., Khan, J. and Sedlacek, R. S., 1980b. Studies on fractionated hyperthermia in experimental animal systems. 1. The foot reaction after equal doses: heat resistance and repopulation. *International Journal of Radiation Oncology, Biology and Physics*, *6*, 1519–1523.

Book review

Fundamental Approaches to Radiologic Special Procedures. A Handbook of Materials, Methods and Techniques. By C. Ody Williams, pp. xx + 164, 1980 (Charles C. Thomas, Springfield, Illinois), $14.95.
ISBN 0-398-04116-4

This is a substantially produced hard-cover manual on approaches to angiography by a radiographic technician who has had the privilege of working with outstanding international radiologists in this field. Thus there is much to expect from the book.

Every vascular investigation is covered systematically and each section consists of a list of equipment, detail on positioning catheter tip, data on the contrast to be injected and the film programme. Each section is completed as briefly as possible yet each contains the maximum information about the items listed. However there is no discussion of any of the technical problems that might be encountered in achieving satisfactory catheter position or how to cope with failure of injector or radiographic apparatus. Illustrations have been excluded deliberately.

The purpose of the book is to help radiology residents know something about special procedures, as well as the radiologists who occasionally do angiograms and the radiographers who have limited experience of angiography but may be called to give assistance in an emergency or in an on-call system. Thus it is a vade mecum of technology.

The value of such a book in a busy department that offers a twenty-four hour service is immediately recognisable, but it is likely to be of greatest benefit to the department of its origin. Other departments will differ, sometimes slightly and sometimes considerably, from the text of this book and though it has much useful information for the tyro, it should be introduced to a department with caution, only after it is known to conform with local practice, for example the volume of contrast agents injected at each site.

One cannot help feeling that any department that needed information of this kind could compile it.

E. Rhys Davies.

1981, *British Journal of Radiology*, *54*, 1091–1093 DECEMBER 1981

Technical notes

Comparison of protocols in the measurement of left ventricular ejection fraction in gated blood-pool scintigraphy

By K. C. Young, B.Sc., Ph.D., M.Inst.P. and R. Railton, B.Sc., Ph.D., F.Inst.P.

Department of Medical Physics, Monklands District General Hospital, Airdrie and
West of Scotland Health Boards, Department of Clinical Physics & Bio-Engineering, 11, West Graham Street, Glasgow

Gated blood-pool scintigraphy (GBPS) has become a well established noninvasive method of measuring the left ventricular ejection fraction (LVEF), which is used to assess patients with a variety of heart conditions (Maisey *et al.*, 1980; Rodger *et al.*, 1980). In addition, the change in LVEF under stress during GBPS is employed as a test for ischaemic heart disease (Borer *et al.*, 1977; Wainwright *et al.*, 1979; Railton *et al.*, 1980). The usefulness of such procedures is, however, limited by the reproducibility of the LVEF measurements. The variability of the LVEF measured is greatly affected by operator decisions, such as the selection of a region of interest (ROI) for background subtraction and the definition of an ROI for the left ventricle. The magnitude of the measured LVEF may also be affected by these decisions.

Modern gamma camera systems are normally supplied with a computer and appropriate software for analysing GBPS studies. In many systems a high degree of automation in the selection of ROI's is used, and it might be expected that these would provide greater reproducibility than those which require more operator intervention. Clearly, a fully automatic protocol will produce identical results when presented with an identical set of data. However, a good automatic protocol must be able to cope with the statistical fluctuations between different sets of data.

In this study we have measured the reproducibility of three edge-detection protocols with varying degrees of automation.

METHODS

Data acquisition

Gated blood-pool studies were carried out as described previously (Young and Railton, 1980).

An *in vivo* red cell labelling technique was used (Pavel *et al.*, 1977). Forty milligrams of Pyrolite (New England Nuclear) were injected intravenously and were followed 20 m later by 740 MBq (20 mCi) ^{99}Tc^{m}-pertechnetate. The subjects lay on a couch under a gamma camera* positioned to achieve optimum separation of the right and left ventricles in the left anterior oblique position (typically 30° with 10° caudal tilt). The ECG signal was used to trigger 16 sequential images during the cardiac cycle. Each image was acquired in a 64×64 data matrix and acquisition was terminated automatically when a total of 300 heart beats had been detected. (This is a typical duration for stress studies). This resulted in an average of 35,000 counts and about 600 matrix elements over the left ventricle. The background activity contributed about 15,000 counts.

Two sequential acquisitions were carried out at rest without altering the relative position of patient to gamma camera, and the data stored on magnetic tape for later analysis. The subjects studied were normal volunteers with a mean age of 27 years.

Data analysis

All the data were analysed by one operator. Each set of data underwent nine-point smoothing. ROI was selected adjacent to the apex of the left ventricle and the average count density in this ROI was subtracted from each matrix element. The LVEF was then calculated using each of the three protocols provided by the manufacturers of the computer.†

Protocol 1. (Rodger *et al.*, 1980). A fixed ROI over the left ventricle was defined by the operator using a light pen. The ejection fraction was then calculated from the difference in counts in this ROI at end-diastole and end-systole.

Protocol 2. (Technicare QMICA). ROI was defined over the left ventricle as for protocol 1. This was automatically divided into four quadrants. A threshold value representing a percentage of the maximum counts in the left ventricle was selected by the operator for each of the four quadrants. This threshold value specified an iso-count contour which defined the edge of the left ventricle in each quadrant

---

*SIGMA-410, Technicare Limited, Rugby.

†VIP450 Video Image Processor, Technicare Limited, Rugby.

TABLE I

COMPARISON OF LEFT VENTRICULAR EJECTION FRACTION (%) MEASUREMENTS FOR THE THREE PROTOCOLS

Patient	Protocol 1			Protocol 2			Protocol 3		
	EF1	EF2	EF2–EF1	EF1	EF2	EF2–EF1	EF1	EF2	EF2–EF1
1	62	65	3	68	69	1	81	84	3
2	62	55	−7	64	60	−4	74	77	3
3	43	43	0	47	48	1	64	63	−1
4	63	57	−6	80	72	−8	82	77	−5
5	43	47	4	47	46	−1	68	69	1
6	72	76	4	86	86	0	86	94	8
7	39	40	1	45	52	7	68	52	−16
8	35	33	−2	39	39	0	44	47	3
9	45	46	1	58	47	−11	84	79	−5
10	40	39	−1	45	48	3	60	51	−9
11	35	38	3	40	41	1	76	70	−6
12	52	50	−2	64	59	−5	77	77	0
Mean of EF2–EF1	−0.2 ± 1.1 (SEM)			−1.3 ± 1.4			−2.0 ± 1.9		
Standard deviation of EF2–EF1	3.6 ± 0.7 (SE)			4.9 ± 1.0			6.5 ± 1.3		
MeanEF	49.2 ± 2.5 (SEM)			56.3 ± 3.0			71.0 ± 2.7		
Standard deviation of EF measurements	2.5 ± 0.5 (SEM)			3.5 ± 0.7			4.6 ± 0.9		

within the original ROI. ROI's for the left ventricle were then calculated by the computer for each of the 16 frames during the cardiac cycle. LVEF was then calculated as for protocol 1. Identical thresholds were selected for both pairs of data analysed.

Protocol 3. (Technicare GMICA). A rectangular ROI was defined by the operator to include all of the left ventricle. The computer then searched for the points of maximum count-density gradient and marked these as the edge of the ventricle. This edge was then smoothed and the area contained defined as the ROI for the left ventricle. The procedure was repeated for each of the 16 gated images. The LVEF was calculated as in protocol 1.

With the same grey-scale settings on the display monitor, each of the protocols was repeated on the two different sets of images for each subject. The standard deviation of the difference between each pair of measurements was calculated. By dividing this by two the standard deviation for LVEF determination was estimated (Young and Railton, 1980).

RESULTS

Table I shows the LVEF measurements on 12 patients using each of the three protocols. The mean LVEF was 49±3% for protocol 1, 56±3% for protocol 2 and 71±3% for protocol 3. Thus, there were highly significant differences ($p < 0.001$; paired t-test) in the magnitude of the LVEF determinations, with protocols 2 and 3 resulting in higher values. The standard deviations for the measurement of LVEF for each of the three protocols are also compared in the table. Protocol 1 had a standard deviation for LVEF determination of 2.5±0.5%. The standard deviation for protocol 2 was 3.5±0.7% which was not significantly greater than for protocol 1. However, protocol 3 had a standard deviation of 4.6±0.9% which was significantly greater ($p < 0.05$; variance ratio test) than protocol 1.

DISCUSSION

This study has demonstrated that there are significant differences in the absolute value of LVEF determined by GBPS according to the analysis procedure. The two techniques which employed a shrinking ROI to follow the left ventricle resulted in higher ejection fractions. This was probably due to the inclusion in the ROI with protocol 1 of activity from outside the ventricle at end-systole. The normal value of the left ventricle ejection fraction obtained with cineangiography is 67% (Dodge and Baxley, 1968) which is in agreement with the results produced by protocol 3. It has previously been shown that a technique with a fixed ROI has an absolute value which is significantly lower than that found with single plane cineangiography whereas methods employing a varying ROI produce values which agree with cineangiography (Taylor *et al.*, 1980).

However, comparison of the different protocols showed that protocol 3 which had the highest degree of automation also had the greatest variability. Since in practice it is changes in ejection fraction that have to be assessed whether due to stress or to changing clinical status, consistency in evaluation is more important than absolute accuracy so that, at present, we utilize protocol 1 in preference to the other protocols.

It is our opinion that protocol 3 is too easily affected by statistical fluctuations in the data, resulting in irregularly-shaped and inconsistent ROI's which do not correspond with the rounded shape of the left ventricle. It may be that a longer acquisition time than that used here would result in better statistical data and allow the automatic procedure to operate more effectively. However, this time is typical of that feasible for GBPS during exercise procedures. Since it is probable that a factor of four in the counts/pixel would be required to produce a noticeable reduction in the statistical fluctuations and since the maximum permissible dose is being administered, acquisition times of about 20 min may be required. This is only possible in non-stress studies although it may not be practical since movement by the patient may distort the images. We also believe that it should be possible to design automatic programs which cope better with statistical fluctuations than those used here.

In the long run, fully automatic analysis procedures will probably take over from the operator-dependent techniques which are still widely used. However, it should be remembered that until these automatic procedures are improved, their reproducibility is by no means guaranteed.

REFERENCES

BORER, J. S., BACHARACH, S. L., GREEN, M. V., KENT, K. M., EPSTEIN, S. E. and JOHNSTON, G. S., 1977. Real-time radionuclide cineangiography in the noninvasive evaluation of global and regional left ventricular function at rest and during exercise in patients with coronary-artery disease. *New England Journal of Medicine*, *296*, 839–844.

DODGE, H. T. and BAXLEY, W. A., 1968. Haemodynamic aspects of heart failure. *American Journal of Cardiology*, *22*, 23–34.

MAISEY, M. N., BRENNAND-ROPER, D. A. and WAINWRIGHT, R. J., 1980. Nuclear medicine in clinical cardiology. *British Medical Bulletin*, *36*, 237–241.

PAVEL, D. G., ZIMMER, A. M. and PATTERSON, V. N., 1977. In-vivo labelling of red blood cells with ^{99}Tc^{m}: a new approach to blood pool visualization. *Journal of Nuclear Medicine*, *18*, 305–308.

RAILTON, R., YOUNG, K. C., DONNELLY, T. and RODGER, J. C., 1980. Cardiac response to graded dynamic exercise assessed by gated blood pool imaging (Abstract). *Nuclear Medicine Communications*, *1*, 163.

RODGER, J. C., RAILTON, R., YOUNG, K. C., LAKHANI, A. K. and GHOURI, M. A. K., 1980. Nuclear angiography in convalescent phase of myocardial infarction: serial study of left ventricular performance. *British Heart Journal*, *43*, 499–505.

TAYLOR, D. N., GARVIE, N. W., HARRIS, D., SHARRATT, G. P., GODDART, B. A. and ACKERY, D. M., 1980. The effects of various background protocols on the measurement of left ventricular ejection fraction in equilibrium radionuclide angiography. *British Journal of Radiology*, *53*, 205–209.

WAINWRIGHT, R. J., BRENNAND-ROPER, D. A., CUENI, T. A., SOWTON, E., HILSON, A. J. W. and MAISEY, M. N. 1979. Cold pressor test in detection of coronary heart disease and cardiomyopathy using technetium-99m gated blood pool imaging. *Lancet*, *2*, 320–323.

YOUNG, K. C. and RAILTON, R. 1980. Inter-observer variation in estimates by nuclear angiography of left ventricular ejection fraction and ejection rate. *British Journal of Radiology*, *53*, 585–588.

An evaluation of count rate losses due to dead time in static and mobile gamma camera data analysis systems

By T. K. Bell, Ph.D., F.Inst.P. and K. Cranley, M.Sc.

Medical Physics Department, Royal Victoria Hospital, Belfast BT12 6BA, Northern Ireland

(Received April 1981 and in revised form September 1981)

ABSTRACT

The count rate responses of a gamma camera and data analysis system have been shown to behave as two separate components. Five systems made up of combinations of two static gamma cameras, two data analysis systems, and a mobile gamma camera system were investigated. Camera and data analysis system dead times are quoted and percentage corrections are plotted against radioactivity of ^{99}Tc^{m} in a patient phantom within the field of view. It is recommended that such a detailed study should be performed for any gamma camera system as part of a quality assurance programme.

Investigations of dead times and count rate losses associated with gamma camera systems include the work of Adams and Zimmerman (1973), Sorenson (1975), Wicks and Blau (1977), Adams *et al.* (1978) and Cranley *et al.* (1980). Studies by the latter investigators are based on the concept that the gamma camera operates as a purely paralysable system and that the associated computerized data analysis unit behaves as a purely non-paralysable system. Having found the dead times, the count rates observed during dynamic radionuclide investigations can be corrected by using the data analysis system. The work included comparison between a two-component model and a one component model, in which the whole system is assumed to behave as paralysable only. It was found that a Searle* LFOV gamma camera on line to a DEC† Gamma-11 data analysis system, with an NC11 interface and utilizing RKO5 magnetic discs, introduced count rate losses additional to those from the gamma camera, and consequently the combined system behaved in a manner described by the two-component model rather than a one-component model.

This current report investigates count rate losses for combinations of the Searle LFOV and Searle Pho-Gamma V gamma cameras on line through the NC11 or the more recent NCV11-A interface to the Gamma-11 system incorporating RKO5 or RKO7 magnetic disc units using the above technique. A Technicare‡ (formerly Ohio Nuclear) mobile gamma camera model Sigma 420 on line to an MCS 560 data analysis unit was also investigated.

THEORY

Examination of the experimental curves of observed count rate plotted against radioactivity for each gamma camera and data analysis system reveals that the two curves do not coincide when further count rate losses are introduced by the second component, the data analysis system (Cranley *et al.*, 1980).

The observed count rate R_0 provided by the gamma camera is related to the true count rate R_t and the paralysable dead time τ_p by

$$R_0 = R_t \exp(-R_t \tau_p) \quad . \quad . \quad . \quad (1)$$

From this, by differentiation of R_0 with respect to R_t

$$\tau_p = 1/R_t^{max} = 1/e.R_0^{max} \quad . \quad . \quad . \quad (2)$$

where e is the exponential constant.

The curve corresponding to the data analysis system output R_0' is a result of τ_p and τ_n, the non-paralysable dead time. Thus

$$R_0' = R_t/[\exp(R_t\tau_p) + (k-1)R_t\tau_p] \quad . \quad (3)$$

where $k = \tau_n/\tau_p$ for $\tau_n > \tau_p$, and $k = 1$ for $\tau_n \leqslant \tau_p$ (Sorenson, 1975). From equation (3),

$$\tau_n = 1/e.R_0^{max} + 1/R_0'^{max} - 1/R_0^{max} \quad . \quad (4)$$

The dead times τ_p and τ_n are calculated from the experimental curves, by reading R_0^{max} from the gamma camera curve and $R_0'^{max}$ from the data analysis system curve. It follows from equation (2) that

$$R_t^{max} = e.R_0^{max} \quad . \quad . \quad . \quad . \quad (5)$$

Thus the activity axis can be calibrated in terms of true count rate.

Assuming that the theoretical curve accurately describes the experimental curve, any experimentally determined count rate may be corrected to yield true count rates by solving equation (3) for R_t, using an iterative computer technique.

METHOD

Each camera system was set up for normal operation and a water tank phantom and polythene bottle sources containing ^{99}Tc^m were utilized in the manner previously described by Cranley *et al.* (1980). Various combinations of collimator, gamma camera, interface and data analysis system were investigated and the one-component and two-component model concepts were applied to each set of experimental data.

RESULTS

Table I shows the six systems from which data were acquired and the corresponding calculated dead times and maximum count rates for the one and two-component models. "Normal" refers to data acquired on the Searle cameras with a console switch position of "normal". "High" refers to the "high count rate" position of this switch.

For Sets 3 and 4 the Pho-Gamma V camera was combined with the NCV11-A interface and different disc and collimator types. One would expect τ_p to be the same, since the present theory depicts the camera only as the paralysable component. For the "normal" switch position, the average value of τ_p is 5.93 μs with a range variation, which is attributed to errors in the method, of ± 0.13 μs. The average value of non-paralysable dead time τ_n is 6.53 μs, with a variation of ± 0.12 μs. Since this is the same size of error as that in τ_p it is concluded that the differences in collimator type and magnetic disc type make little difference to observed dead times in the systems studied.

Comparing Sets 2 and 3 where the only difference is in interface type, average τ_p is 6.16 ± 0.10 μs but there is an obvious change in τ_n and this large difference is attributed to interface type.

Sets 1 and 5 were taken from combinations where the only common apparatus was the LFOV camera. Average τ_p was 5.58 ± 0.32 μs and again the difference in τ_n is pronounced.

---

*Now: Siemens Gammasonics Inc., Illinois, USA.
†Digital Equipment Corporation, Massachusetts, USA.
‡Technicare Corporation, Ohio, USA.

TABLE I

DEAD TIMES AND MAXIMUM COUNT RATES FOUND FOR THE SIX SYSTEMS STUDIED USING TWO-COMPONENT AND ONE-COMPONENT MODELS APPLIED TO EXPERIMENTAL DATA

			Model							
		Count rate switch position	Two-component					One-component		
Set	Gamma camera and data analysis systems		τ_p (μs)	τ_n (μs)	R_o^{max} (kcps)	$R_o'^{max}$ (kcps)	R_t^{max} (kcps)	τ_p (μs)	R_o^{max} (kcps)	R_t^{max} (kcps)
1.	Searle LFOV camera (HRC)* DEC NC11 interface and RKO5 disc	Normal High	5.26 4.21	9.30 8.62	69.9 87.4	54.5 63.1	190.0 237.6	6.75 5.83	54.5 63.1	148.2 171.5
2.	Searle Pho-Gamma V(HSC)† DEC NC11 interface and RKO5 disc	Normal High	6.26 4.68	10.25 8.96	58.8 78.6	47.6 58.8	159.8 213.7	7.73 6.25	47.6 58.9	129.4 160.1
3.	Searle Pho-Gamma V (HSC) DEC NCV11-A interface and RKO5 disc	Normal High	6.06 4.57	6.65 5.49	60.7 80.5	58.6 74.9	165.0 218.8	6.28 4.91	58.6 74.9	159.3 203.6
4.	Searle Pho-Gamma V (HRC) DEC NCV11-A interface and RKO7 disc	Normal High	5.80 4.47	6.41 5.32	63.4 82.3	61.1 76.9	172.3 223.7	6.03 4.79	61.0 76.8	165.8 208.8
5.	Searle LFOV camera (HSC) DEC NCV11-A interface and RKO7 disc	Normal High	5.90 4.42	6.56 5.50	62.4 83.2	59.9 76.4	169.6 226.2	6.14 4.82	59.9 76.3	162.8 207.4
6.	Technicare Sigma 420 (HSC) with MCS 560 unit	—	5.34	$\leqslant \tau_p$	68.9	68.9	187.3	5.34	68.9	187.3

*High resolution collimator.
†High sensitivity collimator.

TABLE II

DEAD TIMES FOUND FOR INDIVIDUAL UNITS USING THE TWO-COMPONENT MODEL

Component	Average dead time (μs)	Dead time type
Searle LFOV	5.58±0.32	Paralysable
Searle Pho-Gamma V	6.04±0.24	Paralysable
DEC Gamma-11 (NC11)	9.77±0.47	Non-paralysable
DEC Gamma-11 (NCV11-A)	6.54±0.13	Non-paralysable

A summary of the dead times averaged for camera type and interface type is given in Table II. A similar trend was observed for τ_p and τ_n when the switch was in the "high count rate" position.

DISCUSSION

The main part of the electronics in each of the two Searle cameras is similar, so it is not surprising that the measured dead times are close. The difference in interface dead time is large and it can be seen that the NCV11-A interface is much faster than the NC11.

Where the NC11 is used, the two-component model is the one which gives the best fit. Where the NCV11-A is used, although according to the present theory the two-component model is correct, the data can be fitted with a one-component model (paralysable only) with approximately the same accuracy in the clinical count rate range, since the extra losses due to the NCV11-A are of the same size as the errors in our method. The major differences in the derived values of R_t^{max} in Table I for Sets 1 and 2 are due to deficiencies in the application of the one-component model to the estimation of true count rates in cases where τ_n is considerably larger than τ_p.

Set 6 was taken using the Technicare camera in its normal mode of operation with a high sensitivity collimator. The data were averaged over five source/phantom configurations. There were no appreciable further losses produced by the MCS 560 data analysis system and therefore

$$\tau_n \leqslant \tau_p = 5.34\ \mu\text{s}.$$

Figures 1 to 6 show the percentage corrections which need to be applied to the observed count rates for the different systems where various activities of ^{99}Tc^m are placed in the fields of view of the gamma cameras. Although activities refer to quantities of

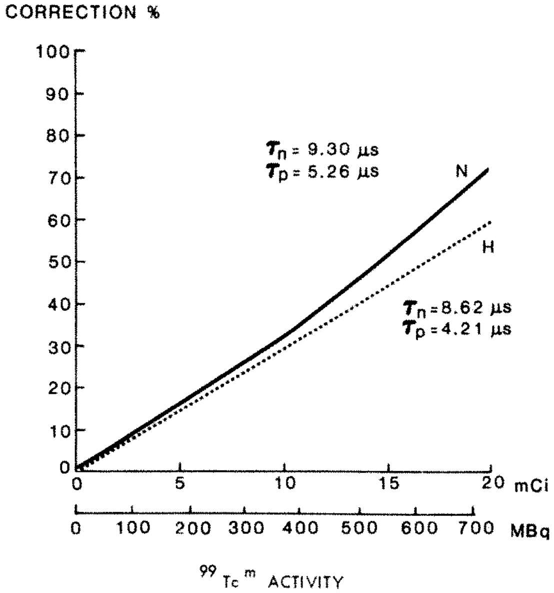


Fig. 1. Searle LFO/RKO5/NC 11/ high resolution.

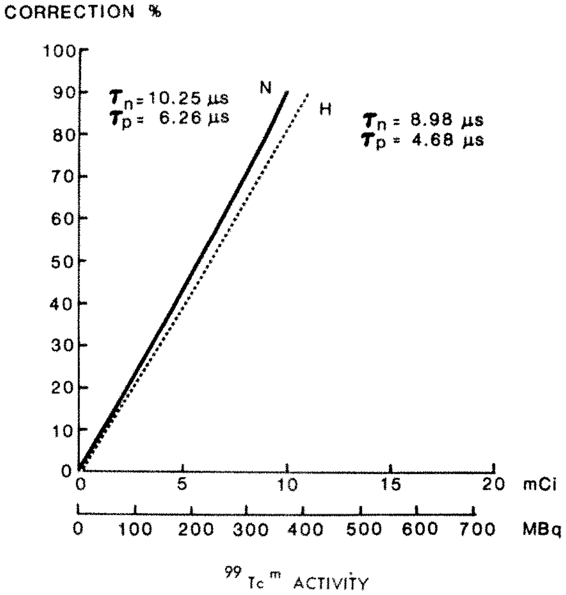


Fig. 2. Searle PGV/RKO5/NC 11/high sensitivity.

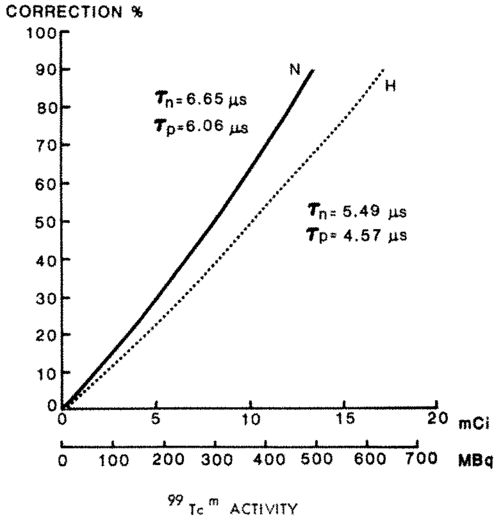


Fig. 3. Searle PGV/RKO5/NCV 11-A/ high sensitivity.

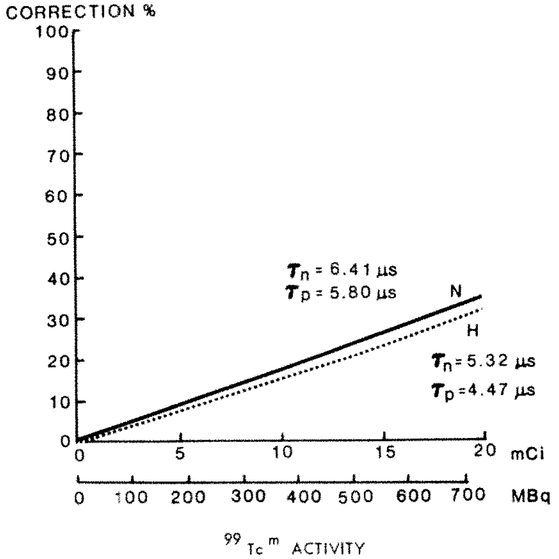


Fig. 4. Searle PGV/RKO7/NCV 11-A/ high resolution.

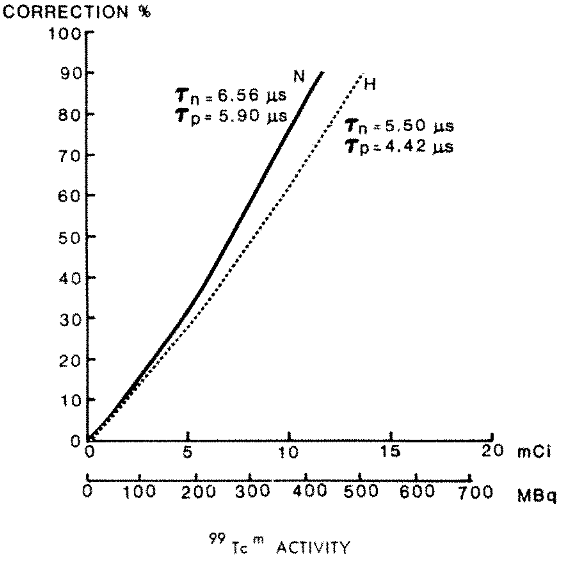


Fig. 5. Searle LFOV/RKO7/NCV 11-A/high sensitivity.

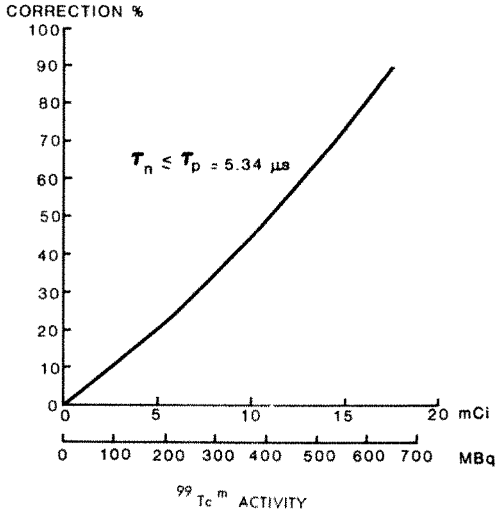


Fig. 6. Technicare Sigma 420/MCS 560/high sensitivity.

Figs. 1–6. Percentage corrections which need to be applied to the observed count rates for the gamma camera and data analysis systems investigated. N = Normal count rate switch position; H = High count rate switch position.

^{99}Tc^{m} within a patient phantom and within the gamma camera field of view, it is possible to estimate the fraction of an injected dose which passes into the field of view. For example, in a first pass cardiac study, one could assume that all the injected radioactivity is seen in the camera field of view, whereas for an ECG-gated cardiac study the heart is visualized after equilibration of the radionuclide in whole body blood and therefore only a fraction of the injected radioactivity is seen within the field of view of the gamma camera.

This will influence the choice of collimator for a given situation. It may be better to use a high resolution collimator for the first pass study, limiting the injected radioactivity to 555 MBq (15 mCi) so that the improved resolution can be utilized with smaller corrections in the observed count rates.

CONCLUSION

It is important to assess the count rates obtained from the main components of gamma camera/computer data analysis systems used for dynamic radionuclide investigations. Considerable variations arise and corrections to provide the true count rates are necessary as indicated by the performance of the three gamma cameras, data analysis systems and interfaces studied. The procedure described enables patient doses and choice of collimator type to be optimized and should form an important part of quality assurance programmes for gamma camera investigations.

REFERENCES

ADAMS, R., HINE, G. J. and ZIMMERMAN, C. D., 1978. Deadtime measurements in scintillation cameras under scatter conditions simulating quantitative nuclear cardiography. *Journal of Nuclear Medicine*, *19*, 538–544.

ADAMS, R. and ZIMMERMAN, D., 1973. Methods for calculating the deadtime of Anger camera systems. *Journal of Nuclear Medicine*, *14*, 496–498.

CRANLEY, K., MILLAR, R. and BELL, T. K., 1980. Correction for deadtime losses in a gamma camera/data analysis system. *European Journal of Nuclear Medicine*, *5*, 377–382.

SORENSON, J. A., 1975. Deadtime characteristics of Anger cameras. *Journal of Nuclear Medicine*, *16*, 284–288.

WICKS, R. and BLAU, M., 1977. The effect of window fraction on the deadtime of Anger cameras: Concise communication. *Journal of Nuclear Medicine*, *18*, 733–735.

Book review

Introduction to Diagnostic Radiology. Ed. by Melvyn H. Schreiber, pp. xiv+368, 156 illus., 1980 (Charles C. Thomas, Springfield, Illinois), $29.50.
ISBN 0–398–0402–5

Medical education is a curious paradox. We choose the most intelligent students we can find and tell them that a university is a place for thinking, discussion and learning. We then proceed to stuff them with facts like geese destined to become paté de foie gras, and discourage them from asking questions. With every speciality fighting for its share of the curriculum time, radiology everywhere is struggling to establish its place in the syllabus; this needs to be done since the student when qualified will be trying to interpret films daily. How often will he plate out or identify the organism in pus?

Books written for medical students tend to mirror departmental teaching methods. Some try to relate radiology to clinical problems, some to lay down rules, others to explain basic radiological principles so that the student can recognize the normal and the more common abnormalities.

This book, edited by Professor Schreiber of the University of Texas, consists of 11 chapters written by ten contributors. Uniformity of presentation is achieved by a standard approach, with the chapter on each anatomical area covering the possible diagnostic alternatives, followed by a suggested radiological work up for common conditions and ending with study questions and answers. Most of the text in each chapter is concerned with methods of investigation, illustrated with interesting examples of diseases that are not always common. In the chapter on the lungs there are 12 figures, three containing examples of ultrasound scans, which may give the student a misleading idea of its value in the chest. Overall this book seems to me to fall into the category of didactic lecturing, and could be summarized as advising the student that radiology is difficult so when he has a diagnostic problem he should ask a radiologist how best to investigate it. In case this was too simple a summary I asked an English medical student for her opinion, which she has allowed me to give here.

"The book is written to 'introduce medical students to the radiological studies available for the solution of diagnostic problems.' Emphasis is placed on suggesting the best investigation to order for some symptoms and signs associated with particular organ systems. However, it would be helpful if each section started with a series of normal X rays to refer to when looking at abnormal ones, and had more illustrations been included of the abnormalities described in the text. The chapter on the heart and great vessels was particularly well set out and seems to have the balance right.

"While the aim of the book is fulfilled, it is questionable as to whether this is the right target to have in mind when writing a radiology textbook for students. As a medical student I would have found it more useful if basic X-ray interpretation had been explained and common normal and abnormal X-ray appearances shown rather than the more advanced investigations. These are usually done at the radiologist's suggestion after the basic X-ray films have been discussed."

We seem to be in agreement.

HEATHER BURKE,
W. D. JEANS.

1981, *British Journal of Radiology*, *54*, 1098–1100

Case reports

CT scan appearances in a patient with lipoid proteinosis

By J. N. Leonard and T. J. Ryan

Department of Dermatology, The Slade Hospital

and P. W. E. Sheldon

Department of Neuroradiology, The Radcliffe Infirmary, Oxford

(*Received June 1981*)

Lipoid proteinosis is a rare disorder and is inherited in an autosomal recessive pattern. It was first described in 1929 (Urbach and Wiethe) and since then about 200 cases have been reported, mainly in patients with a known European ancestry. The pathogenesis is unknown; the only constant feature is deposition of an amorphous hyaline material that stains with PAS reagent in the affected tissues. These include in particular the mucous membranes of the mouth and larynx and the skin, though other organs may be involved (Hofer, 1973; Heyl, 1963).

Laryngeal involvement leads initially to hoarseness—an inability to cry from birth often being one of the first signs of the disease. Laryngeal obstruction is a rare cause of death in affected patients; the prognosis otherwise is good. Infiltration of the mouth and pharynx leads to dry cracked lips and tethering of the tongue. During the first two decades of life diffuse infiltration occurs in the skin. Yellow or brown papules appear on the face giving a waxy look to the tissue. Beaded papules along the eyelids are characteristic. A non-scarring alopecia may develop (Fig. 1). Nodular lesions also occur on the elbows and knees where they may form warty plaques (Fig. 2). Perifollicular atrophy of the neck and upper arms may cause a mistaken diagnosis of pseudo-xanthoma elasticum. Various congenital abnormalities such as aplasia of the incisor teeth have been reported. Epilepsy with associated intracranial calcification is a feature in a significant proportion of patients.

Radiological interest has centred around abnormalities of the skull radiograph. For many years there was dispute as to whether the calcification was situated in the vessels, the meninges or the brain. Sheldon maintained that the lesion lay in the

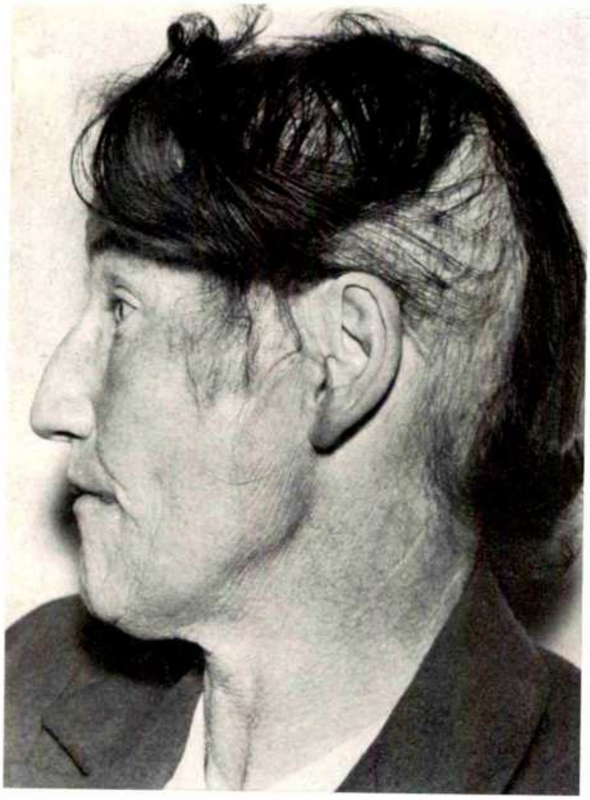


FIG. 1.
Waxy appearance to face and non-scarring alopecia.

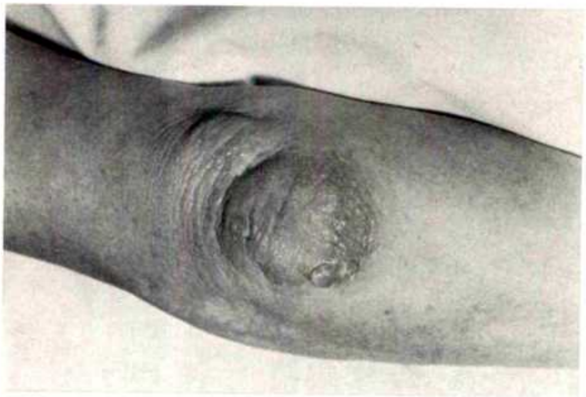
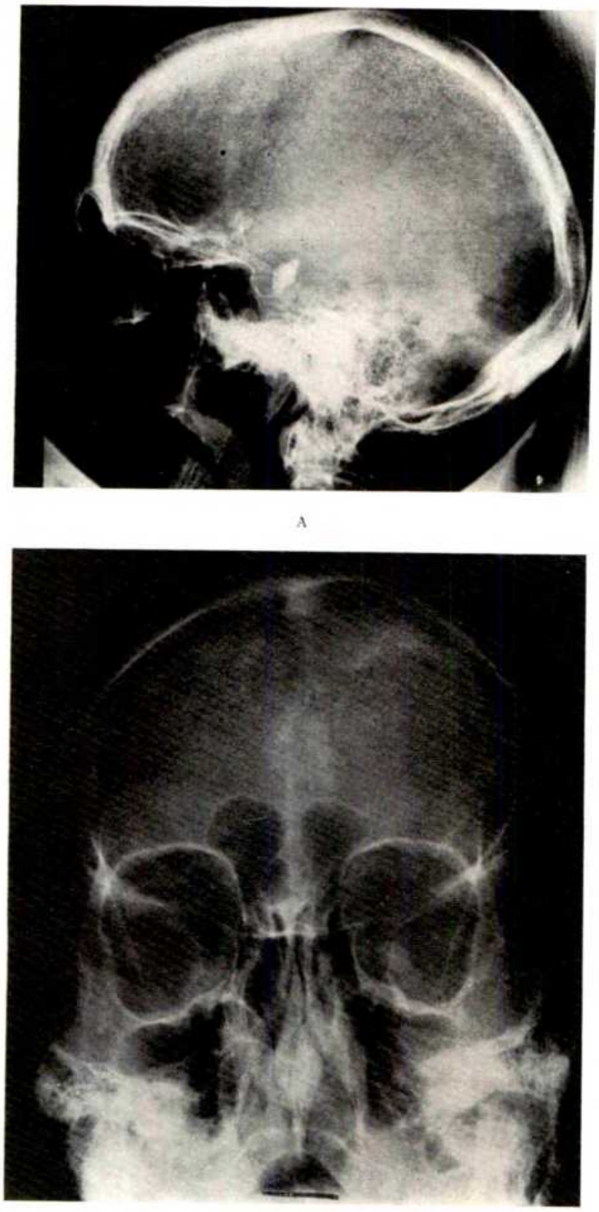


FIG. 2.
Warty plaque on elbow.

brain (Cowan *et al.*, 1961). More recently post-mortem reports have indeed shown it to be intracerebral involving the hippocampus and the amygdaloid nucleus bilaterally (Holtz, 1962; Meenan *et al.*, 1978). This paper reports the use of CT scanning in localizing the calcification during life.

CASE REPORT

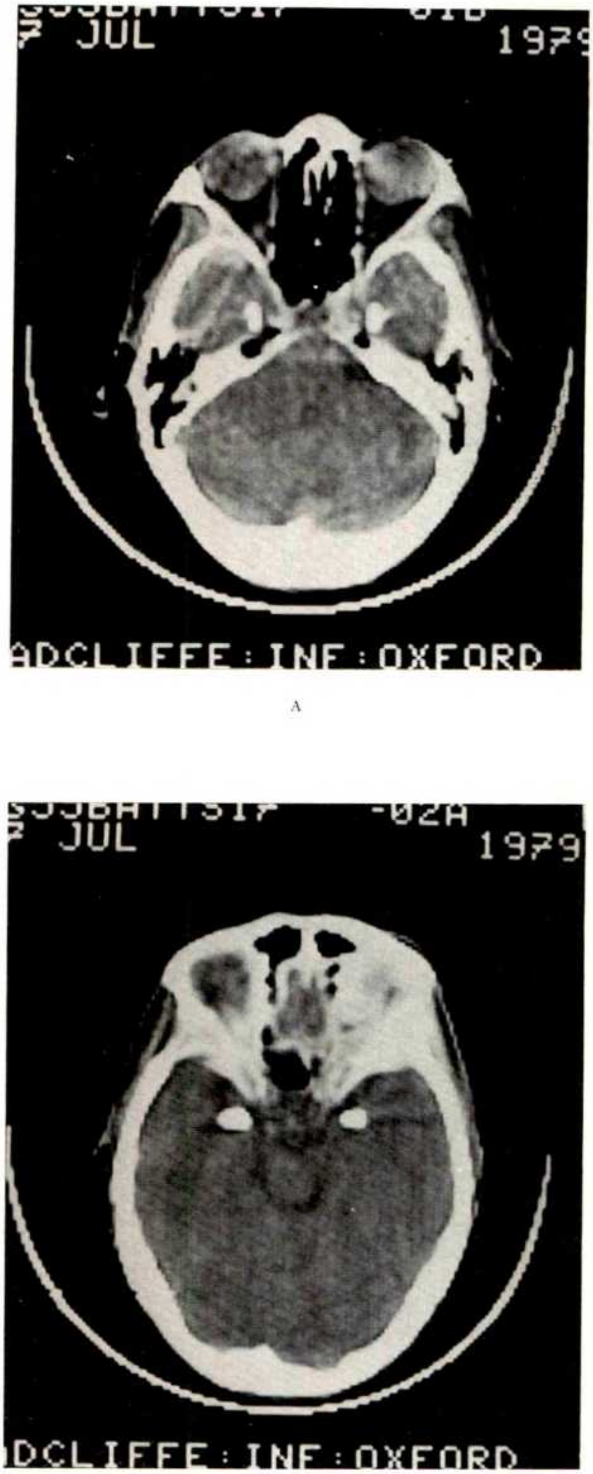
The patient concerned was the first case of lipoid proteinosis to be described in Britain (Cowan *et al.*, 1961). Her


A

B

FIG. 3.

(A, B) Showing the two discrete nodules on either side.



A

B

FIG. 4.

(A, B) Sections through the calcified nodules and confirming position in the temporal lobe.

1981, *British Journal of Radiology*, *54*, 1100–1102

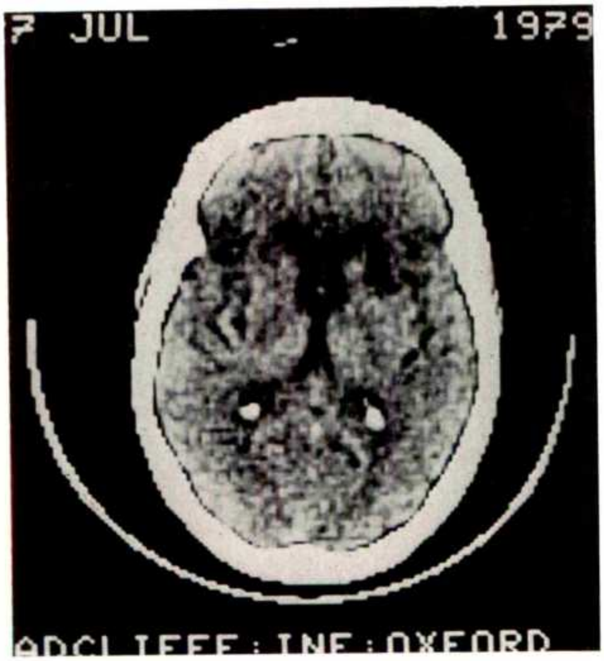


FIG. 4C.

Higher cut showing the general involutional changes, and infarction in the anterior limb of the right internal capsule.

neurological problems began in 1956 at the age of 40 when she was diagnosed as having akinetic epilepsy. This has been easily controlled on phenytoin. More recently she has developed a peripheral neuropathy of unknown cause. It has been suggested that her nervous system has become diffusely infiltrated with hyaline material though we have been unable to prove this.

INVESTIGATIONS

Skull radiograph (Fig. 3) showed the intracranial calcification overlying the pituitary fossa in the lateral view, but lying about 2.5 cm. from the mid-line on either side. Tomography showed each calcification to consist of two discrete symmetrical areas close to each other.

CT scan confirmed the presence of two calcifications on either side (Fig. 4). These lie intracerebrally in the region of the hippocampi or amygdaloid nuclei. Also there are widespread involutionary changes and evidence of an old infarct close to the head of the right caudate nucleus.

DISCUSSION

The CT scan of this patient shows intracerebral calcification in the area of the hippocampus. This is consistent with the post-mortem reports and supports our original interpretation of the skull radiographs. The localization in this area of the brain does not give rise to a specific clinical pattern of epilepsy. Temporal lobe fits, grand and petit mal have all been reported (Hofer, 1973).

REFERENCES

COWAN, M. A., ALEXANDER, S., VICKERS, H. R. and COWDELL, R. H., 1961. Case of lipoid proteinosis. *British Medical Journal*, *ii*, 557–560.

HEYL, T., 1963. Lipoid proteinosis. *British Journal of Dermatology*, 75, 465–477.

HOFER, P. A., 1973. Urbach-Wiethe disease: a review. *Acta Dermato-Venereologica*, *53*, suppl. 71.

HOLTZ, K. H., 1962. Über Gehirn und Augenveränderungen bei Hyalinosis cutis et mucosa (lipoid proteinosis) mit Autopsiefund. *Archiv für klinische und experimentelle Dermatologie*, *214*, 289–806.

MEENAN, F. O. C., BOWE, S. D., DINN, J. J., MCCABE, M., MCCULLEN, O., MASTERSON, J. G. and TOWERS, R. P., 1978. Lipoid proteinosis: a clinical pathological and genetic study. *Quarterly Journal of Medicine*, *47*, 549–561.

URBACH, E. and WIETHE, C., 1929. Lipoidosis cutis et mucosa. *Virchows Archiv für pathologische Anatomie und Physiologie*, *273*, 285–319.

Recurrent non-surgical pneumoperitoneum due to spontaneous pneumothorax

By S. Fataar, F.R.C.R., F.F.Rad.(D) (S.A.), P. Morton, F.F.Rad.(D) (S.A.) and
A. Schulman, M.R.C.P., F.R.C.R.

Department of Radiology, Groote Schuur Hospital/University of Cape Town, Observatory, Cape Town 7925, South Africa

(*Received May 1981*)

The presence of subphrenic air in a patient who has not recently undergone abdominal surgery does not always indicate a surgical emergency due to perforated bowel. In such a patient, the absence of a clinically acute abdomen allows designation of this innocent pneumoperitoneum as the non-surgical pneumoperitoneum (Gantt *et al.*, 1977) or pneumoperitoneum without peritonitis (Felson and Wiot, 1973). The causes include peritoneoscopy, peritoneal aspiration, peritoneal dialysis, diaphragmatic dissection in cardiac surgery (Glanz *et al.*, 1978) and pneumatosis cystoides intestinalis (Wollock *et al.*, 1972). In females, transvaginal entry of air has resulted from douching, squatting in the puerperium or sexual stimulation by blowing (Gantt *et al.*, 1977; Krausz and Manny, 1977; Felson and Wiot, 1973).

Where pneumoperitoneum and pneumothorax coexist, the usual cause is assisted ventilation (Macklin and Macklin, 1944; Donahoe *et al.*, 1972). The increased intrapulmonary pressure causes alveolar rupture with dissection of air along the vascular sheaths to the mediastinum. Upward extension of the pneumomediastinum results in surgical emphysema of the neck. Downward extension of the pneumomediastinum results in air tracking to the retroperitoneal tissues via the oesophageal, aortic and caval hiati. The retroperitoneal air may rupture through into the peritoneal cavity to produce a true pneumoperitoneum or track subphrenically in the extraperitoneal space to mimic free intraperitoneal air (Schulman *et al.*, 1981). Alveolar rupture with assisted ventilation may also be associated with rupture through pleura to cause a pneumothorax.

CASE REPORT

A 28-year-old mentally retarded male, suffering from a dysmyelinating disease, presented with a four-day history of herpetic oral ulcers and sudden onset of dyspnoea and pleuritic right chest pain. On examination there were decreased breath sounds in the right chest. The abdomen was soft with normal bowel sounds. The chest radiograph revealed a moderate-sized pneumothorax on the right and air under the diaphragm (Fig. 1). The slightly collapsed right lung had a few small sub-pleural blebs in the upper zone. The bowel pattern was normal on the abdominal radiograph and air was established as being intraperitoneal as air moved around freely to lie under the liver on prone view (Fig. 2) and along the lateral abdomen on decubitus view. There was no evidence of retroperitoneal air, pneumomediastinum or surgical emphysema. Following 48 hours of underwater drainage of the right hemithorax, both the pneumothorax and pneumoperitoneum had cleared.

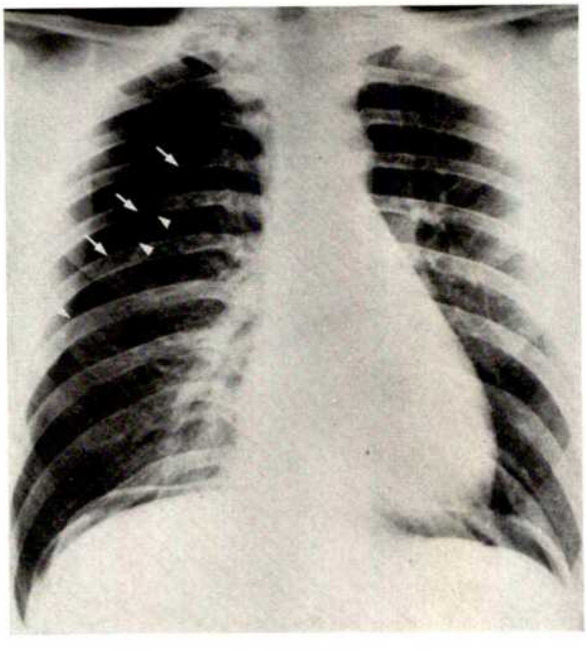


FIG. 1.

Erect chest radiograph showing pneumoperitoneum, right pneumothorax (straight arrows) and subpleural blebs (arrow heads). There is no pneumomediastinum.

Two months later, while asymptomatic, a follow-up chest radiograph again revealed a combined right pneumothorax and pneumoperitoneum, both of which settled with drainage. On his third admission six months later with right-sided chest pain lasting a month, he had only a moderate pneumothorax and no air under the diaphragm. He again settled after drainage.

Four months later he returned with fulminating urinary sepsis and died four weeks later. During that time frequent chest radiographs appeared normal. Autopsy revealed numerous subpleural blebs in both lung apices while the stomach and small and large bowel appeared normal. The diaphragm was not thoroughly examined, but no obvious defects were noted.

DISCUSSION

Pneumoperitoneum secondary to spontaneous pneumothorax has not been recorded previously whereas pneumothorax following pneumoperitoneum has resulted from perforated peptic ulcer (Nayak and Lawrence, 1976; Bradley and Fielding, 1972), induced pneumoperitoneum (Smith, 1943), pelvic gynaecography (Seltzer, 1976) and peritoneoscopy (Glauser and Bartlett, 1974). None of these had any evidence of retroperitoneal or mediastinal air and the only explanation is that there is a direct communication across the diaphragm. This may result from a ruptured diaphragm and a history of lower chest or abdominal trauma would favour this as a cause and may be found without any abdominal

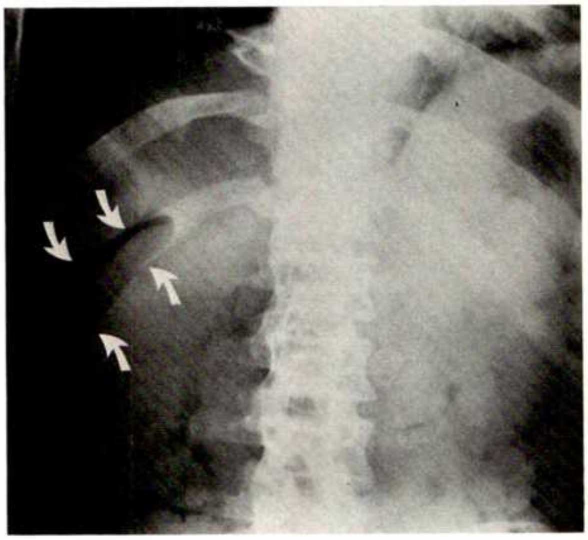


FIG. 2.

Prone abdominal radiograph showing free intraperitoneal air under the liver (arrows). There is no retroperitoneal air.

1981, *British Journal of Radiology*, *54*, 1102–1104

visceral herniation into the chest (Fataar and Schulman, 1979). The absence of any previous trauma favoured congenital pleuroperitoneal fistulation as the cause in our patient.

Unilateral and bilateral small holes have been found in the diaphragm at autopsy and laparotomy and may be solitary or multiple (Smith, 1943; Nayak and Lawrence, 1976; Bradley and Fielding, 1972; Liebermann *et al.*, 1966). These congenital fistulae are small which may account for them being missed at autopsy in our patient when they were not specifically sought. These defects also allow fluid transit across the diaphragm and accounted for 5.5% of Liebermann *et al.*'s cirrhotic patients with ascites having hydrothoraces. Finn and Jowett (1970) recorded an acute hydrothorax repeatedly complicating every attempt at peritoneal dialysis in one patient.

In our patient the spontaneous pneumothorax was probably due to the subpleural blebs, the commonest cause of spontaneous pneumothorax which recurs ipsilaterally in 30% (Felson and Wiot, 1973; Greene *et al.*, 1977). It is unlikely that the pneumoperitoneum preceded the pneumothorax, as the symptoms were thoracic only with a clinically normal abdomen and normal abdominal viscera found at autopsy, when the blebs seen in the partially collapsed lung on the chest radiographs were confirmed.

ACKNOWLEDGMENTS

We thank Miss B. Neumann for secretarial assistance and Mrs. J. Tuft for the photography.

REFERENCES

BRADLEY, J. W. P. and FIELDING, L. P., 1972. Hydropneumothorax complicating perforated peptic ulcer. *British Journal of Radiology*, *59*, 72–73.

DONAHOE, P. K., STEWART, D. R., OSMOND, J. D. and HENDREN, W. H., 1972. Pneumoperitoneum secondary to pulmonary air leak. *Journal of Pediatrics*, *81*, 797–800.

FATAAR, S. and SCHULMAN, A., 1979. Diagnosis of diaphragmatic tears. *British Journal of Radiology*, *52*, 375–381.

FELSON, B. and WIOT, J. F., 1973. Another look at pneumoperitoneum. *Seminars in Roentgenology*, *8*, 437–443.

FINN, R. and JOWETT, E. W., 1970. Acute hydrothorax complicating peritoneal dialysis. *British Medical Journal*, *ii*, 94.

GANTT, C. B., DANIEL, W. D. and HALLENBECK, G. A., 1977. Nonsurgical pneumoperitoneum. *American Journal of Surgery*, *134*, 411–414.

GLANZ, S., RAVIN, C. E. and DEREN, M. M., 1978. Benign pneumoperitoneum following median sternotomy incision *American Journal of Roentgenology*, *131*, 267–269.

GLAUSER, F. L. and BARTLETT, R. H., 1974. Pneumoperitoneum in association with pneumothorax. *Chest*, *66*, 536–540.

GREENE, R., MCLOND, T. C. and STARK, P., 1977. Pneumothorax. *Seminars in Roentgenology*, *12*, 313–325.

KRAUSZ, M. and MANNY, J., 1977. Pneumoperitoneum associated with pneumothorax: a surgical dilemma in the post-traumatic patient. *Journal of Trauma*, *17*, 238–240.

LIEBERMANN, F. L., HIDEMURA, R., PETERS, R. L. and REYNOLDS, T. B., 1966. Pathogenesis and treatment of hydrothorax complicating cirrhosis with ascites. *Annals of Internal Medicine*, *64*, 341–351.

MACKLIN, M. T. and MACKLIN, C. C., 1944. Malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions: an interpretation of the clinical literature in the light of laboratory experiment. *Medicine*, *23*, 281–358.

NAYAK, I. N. and LAWRENCE, D., 1976. Tension pneumothorax from a perforated gastric ulcer. *British Journal of Surgery*, *63*, 245–247.

SCHULMAN, A., FATAAR, S., VAN DER SPUY, J. W., MORTON, P. C. G. and CROZIER, J., 1981. Air in funny places: some causes and ramifications of pneumomediastinum (submitted to *Clinical Radiology*).

SELTZER, R. A., 1976. Pneumothorax complicating pelvic pneumography. *British Journal of Radiology*, *49*, 892.

SMITH, C. N., 1943. Induced pneumoperitoneum: a fatal case. *British Medical Journal*, *ii*, 404.

WOLLOCK, Y., DINTSMAN, M. and WEISS, A., 1972. Pneumatosis cystoides intestinalis of adulthood. *Archives of Surgery*, *105*, 723–726.

Iatrogenic (self-induced) wet beri-beri

By R. W. Saleh, D.M., D.M.R.E., M.D.
Itobba Hospital, Cairo, Egypt

N. G. Ghaly, M.B., B.Ch., D.M. and M. H. Aziz, M.B., B.Ch.
The American Hospital, Tanta, Egypt

(*Received May 1981*)

Beri-beri used to be a common disease in tropical and sub-tropical areas as well as in the crews of ships on the high seas (Wilcocks and Manson-Bahr, 1972). Nowadays, however, it is uncommon and the wet type even rare. In western countries the dry type is rarely encountered and is invariably associated with chronic alcoholism. It is thus identified as a conditioned deficiency disease (Scott, 1978). Generally, however, beri-beri in both childhood and adulthood is present in association with protein-calorie malnutrition (Moran and Greene, 1979).

Beri-beri is caused by deficiency of vitamin B_1

Reprint requests: Dr. M. H. Aziz, Department of Radiology, The American Hospital, Tanta, Egypt.

(aneurin or thiamine). The pyrophosphate ester of thiamine is a co-carboxylase which catalyses the decarboxylation and oxidation of pyruvic acid in living matter, and is thus involved in the metabolism of carbohydrates in the Krebs citric acid cycle (Wilcocks and Manson-Bahr, 1972). In deficiency of vitamin B_1, the tissues which use glucose in large amounts as a primary source of energy are most markedly affected. Thus the nervous tissues and heart bear the main brunt of the disease. In nervous tissues, degenerative changes ranging from slight medullary changes to complete destruction of the nerve may occur. In heart muscle, water retention leads to loss of contractility which is reflected clinically as high output cardiac failure (Scott, 1978; Wilcocks and Manson-Bahr, 1972). The right side of the heart is more affected than the left. Oliguria of high specific gravity with no albumin, and generalized oedema are common features. Pleural effusions, unilateral or bilateral are also common.

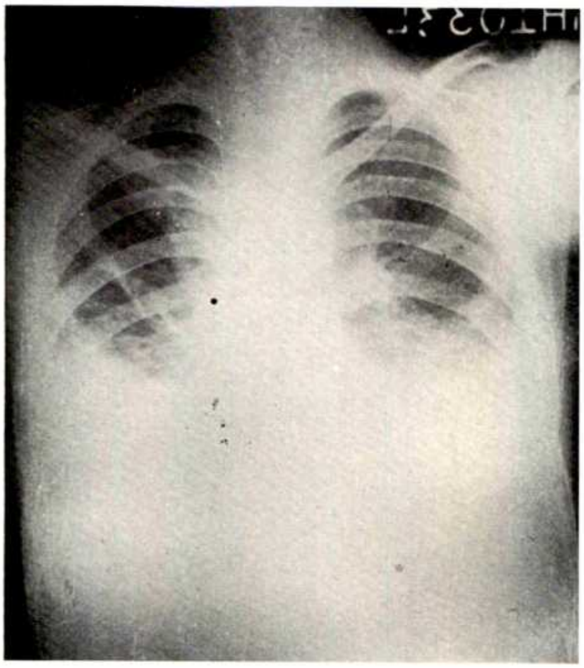


FIG. 1.
Bilateral pleural effusions.

CASE REPORT

A 16-year-old male presented with loss of 30 kg bodyweight within one year, oedema most marked in the lower limbs, dyspnoea on exertion, orthopnoea and skin pigmentation. One year before he presented to us, he suffered an attack of diarrhoea and vomiting which was diagnosed as

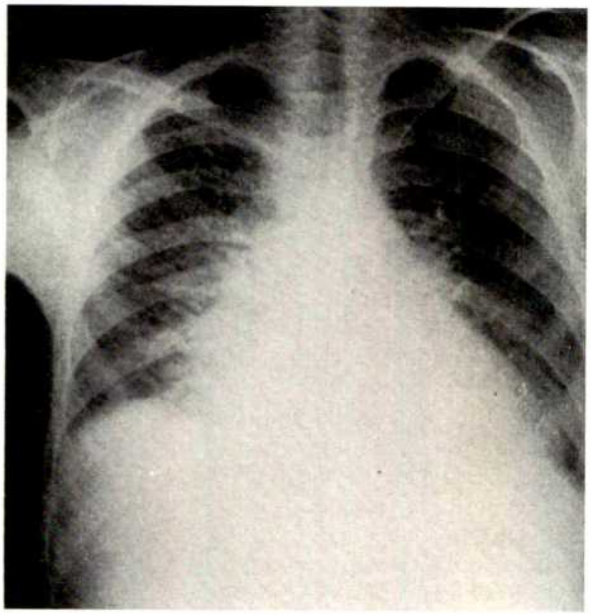


FIG. 2.
Pleural effusions resolved. Enlarged heart and pulmonary oedema are still seen.

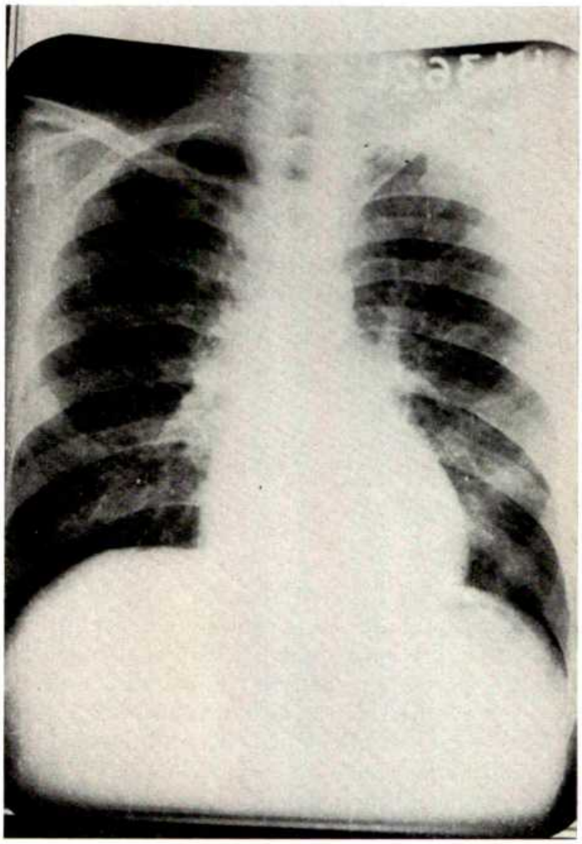


FIG. 3.
Normal chest and heart. Two weeks after starting treatment with vitamin B_1.

1981, *British Journal of Radiology*, *54*, 1104–1107

enterocolitis, and was treated with intestinal antibacterial and antiamoebic drugs and controlled diet. Relapse of diarrhoea occurred, which the patient treated himself by abandoning the prescribed balanced diet and continuing to eat white bread, boiled polished rice and boiled vegetables only. Six months later he began to notice oedema of his legs and dyspnoea on exertion, as well as brownish discoloration of the skin.

On presentation, his pulse rate was 130/min and BP was 110/90. Pellagric rash, pitting oedema, marked pallor and emaciation were present. There were bilateral pleural effusions, ascites, enlarged soft spleen and liver and congested, pulsating neck veins. Oliguria without albumin or casts was noted and there was marked anaemia (9g 46%) hypoproteinaemia (3 g% total proteins). The ESR and stools were normal. Chest radiography confirmed the presence of bilateral pleural effusions (Fig. 1), and a barium follow-through examination showed normal findings. He was treated by high protein diet, oral iron, folic acid, nicotinic acid, vitamin B complex and vitamin C, as well as four transfusions of packed red cells and diuretics.

Three weeks later, anaemia and hypoproteinaemia were improved and the oedema had disappeared but the patient was still dyspnoeic and orthopnoeic. A chest radiograph showed absorption of the pleural effusions, but a markedly enlarged heart and interstitial pulmonary oedema were seen (Fig. 2). Thus the possibility of beri-beri of the wet type was suggested. Diuretics were then stopped and vitamin B_1 100 mg tds started and vitamin B complex and vitamin C and iron were continued. Marked clinical improvement was noticed within one week. A chest X-ray two weeks after initiation of vitamin B_1 treatment was normal (Fig. 3). Three days later the patient was discharged from hospital.

DISCUSSION

The full picture of wet beri-beri is seen in this case. It is believed to be self-induced, resulting from prolonged abstention from proteins, fresh vegetables and fruits. The association of thiamine deficiency with low protein-calorie diet is known (Moran and Greene, 1979), as well as the association of poor intestinal absorption of thiamine with folate depletion (Thompson and Leevy, 1971).

The marked rapid improvement resulting from the use of vitamin B_1 treatment alone confirmed the aetiology of the condition.

REFERENCES

MORAN, J. R. and GREENE, H. L., 1979. The B vitamins and vitamin C in human nutrition. I. General considerations and obligatory B vitamins. II. Conditional B vitamins and vitamin C. *American Journal of Diseases of Children*, *133*, 192–199, 308–314.

SCOTT, SIR RONALD BODLEY, 1978. Beri-beri heart disease. In *Heart diseases in various systematic diseases: Price's Text Book of The Practice of Medicine*. 13th edit. (Oxford University Press, London), p. 779.

THOMPSON, A. D. and LEEVY, C. M., 1972. Observations on the mechanism of thiamine hydrochloride absorption in man. *Clinical Science*, *43*, 153–163.

WILCOCKS, C. and MANSON-BAHR, P. E. C., 1972. Vitamin deficiencies: beri-beri. In *Manson's Tropical Diseases*. 17th edit. (Bailliere Tindall, London), pp. 763–770.

Technetium 99m-diethyl-IDA hepatobiliary scintigraphy in the pre-operative diagnosis of choledochal cyst

By M. Paramsothy, M.B., B.S., M.R.C.P. (UK) and
K. Somasundram, M.B., B.S., F.R.C.S. (Edin. & Eng.), F.R.A.C.S.

Departments of Radiology and Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

(Received April 1981)

Choledochal cyst, first described by Vater (1728), is a localized cystic dilation of the common bile duct and may extend upwards to involve the hepatic ducts. The disease is relatively rare and affects orientals more frequently than any other race (Han *et al.*, 1969). Early diagnosis and treatment can prevent the complications of ascending cholangitis, calculus formation, spontaneous or traumatic rupture, biliary cirrhosis, portal hypertension, varices, carcinoma of the cyst wall and death (Barlow *et al.*, 1976). The clinical triad of abdominal pain, jaundice and abdominal mass is present in only about 20% of the cases and unless the index of suspicion is high the diagnosis will be missed (Alonso-Lej *et al.*, 1959). Intravenous cholangiogram may be diagnostic in the absence of jaundice (Alonso-Lej *et al.*, 1959), and ultrasonogram could be helpful in demonstrating the presence of a cyst, although it is not always diagnostic (Barlow *et al.*, 1976). After Williams *et al.* (1970) first reported a choledochal cyst diagnosed by hepatoscintigraphy, iodine 131 Rose Bengal liver scan appeared to be the only consistent investigation of diagnostic value (Barlow *et al.*, 1976). The physical characteristics of ^{131}I are not optimal for imaging and its relatively long half-life and its β emissions result in a relatively high radiation dose to the bowel mucosa which finally prevented its widespread use. Iodine 123 overcomes this limitation but is expensive and, because of its physical half-life of 13 hours, not practical for unscheduled emergency examinations.

Technetium 99m, because of its excellent physical

Request for reprints: Dr. M. Paramsothy, Department of Radiology, University of Malaya, Kuala Lumpur, Malaysia.

characteristics for imaging, its easy availability and its short half-life of six hours and thus lower radiation dose, is now the radionuclide of choice. Many complexes of ^{99}Tc^{m} have been used for hepatobiliary imaging including penicillamine, dihydrothioctic acid (DHT), tetracycline, mercaptoisobutyric acid (MIBA) and pyridoxylideneglutamate (PYG). The recently developed iminodiacetic acid (IDA) derivatives appear to be superior and the most promising agents (Harvey *et al.*, 1975). Diethyl-IDA (EHIDA), because of its faster blood clearance and lower renal excretion, appears to be superior to dimethyl-IDA (HIDA) (Wistow *et al.*, 1977). The purpose of this paper is to demonstrate the excellent diagnostic value of ^{99}Tc^{m}-diethyl-IDA hepatobiliary imaging in choledochal cyst.

CASE REPORTS

Case 1.

A six-year-old Chinese girl was admitted to the paediatric unit of the University Hospital on November 25, 1980 for evaluation of a mass in the right upper abdomen. There was no history of abdominal pain, vomiting, diarrhoea or jaundice. She had no previous history of jaundice or any other significant illnesses.

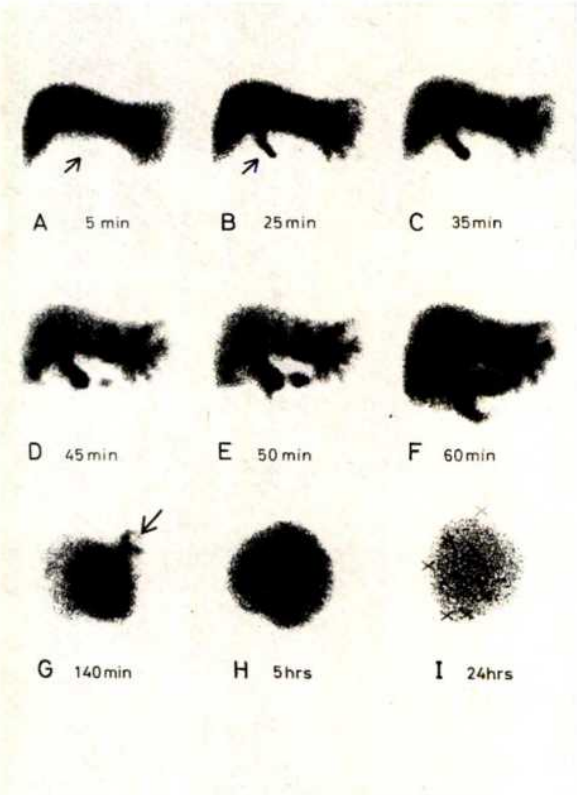


FIG. 1. *Case 1.*

Pre-operative ^{99}Tc^{m}–EHIDA hepatobiliary scan. Filling defect in the liver (A–D), filling of choledochal cyst (E–I).

On examination she was normally developed, thin, afebrile and not jaundiced. The only physical abnormality discovered was a mass in the right upper quadrant of the abdomen which was about 4 × 4 cm and firm and smooth to palpation. The liver and spleen were not palpable.

Her haemoglobin, white cell count, blood urea and electrolytes, and urinalysis were within normal limits. Except for an elevated alkaline phosphatase of 396 IU/l, her liver function test was normal.

Ultrasonogram demonstrated a large transonic area within the liver and was reported as a hepatic cyst. An initial liver scan performed with ^{99}Tc^{m}-tin colloid showed a large defect in the inferior aspect of the right lobe.

Sequential scintigraphy with ^{99}Tc^{m}-EHIDA revealed the filling defect in the right hepatic lobe (Fig. 1A–D) that became an area of concentration of the radiopharmaceutical on the subsequent serial scans (Fig. 1I). The delayed scans at five hours and at 24 hours showed good concentration of the radionuclide in the choledochal cyst and no excretion into the gut (Fig. 1H, I).

At laparotomy, a large choledochal cyst involving the common bile duct containing 400 ml of bile was seen. Excision of the cyst, cholecystectomy and hepatico-jejunostomy with Roux-en-Y anastomosis was performed. She made an uneventful recovery and a post-operative ^{99}Tc^{m}-EHIDA scan showed filling of the initial defect in the liver and prompt excretion of tracer into the gut through the biliary anastomosis. No bile leak or bile stasis were demonstrated in the anastomosed intestinal segment. Prompt clearance of bile from the jejunal anastomosis was also seen.

Case 2.

A 34-year-old Chinese female was referred on January 6, 1981 for evaluation of a large choledochal cyst. She had been in good health until six years ago when immediately after delivery of her first baby she had intermittent pain and swelling in her right upper abdomen. The swelling was less in the morning but became more prominent towards the evening. There was no fever or jaundice and with symptomatic treatment the pain and swelling subsided completely within a week. She had two further similar episodes when she delivered her second and third babies. On both these occasions the pain and swelling subsided completely within a week, and no diagnostic investigations were carried out. In December 1980 she was admitted to her local hospital with severe right abdominal pain. She was found to have a low-grade fever, and a tender swelling in the right upper abdomen but no jaundice. She was treated conservatively for acute cholecystitis and the fever, pain and tenderness soon subsided. However, the swelling continued to persist, being more prominent in the evening than in the morning. She had no other symptoms. A plain abdominal radiograph showed a small opacity in the right hypochondrium. An intravenous cholangiogram showed a normal sized gall bladder. Barium meal series were reported as normal.

On examination she was normally developed and slightly obese. The only physical abnormality found was a large, non-tender, firm, smooth mass in the right upper abdomen, extending to the level of the umbilicus.

Her haemoglobin, white cell count, blood urea and electrolytes, urinalysis and liver function tests were within normal limits. Ultrasonogram demonstrated a large cyst with a distended gall-bladder but was not diagnostic. No gall-stones were seen. Technetium 99m–EHIDA hepatobiliary scintigraphy revealed excretion of the radionuclide by the liver and its concentration in the initial area of filling defect in the right lobe noted in the hepatic phase (Fig. 2). A delayed scan at 160 min and five hours showed good concentration of the radiopharmaceutical in the large choledochal cyst (Fig. 2C, D).

At laparotomy a large choledochal cyst containing 1 l of concentrated bile was seen. Excision of the cyst, cholecystectomy, and hepatico-jejunostomy with Roux-en-Y anastomosis were done. She had an uneventful post-operative

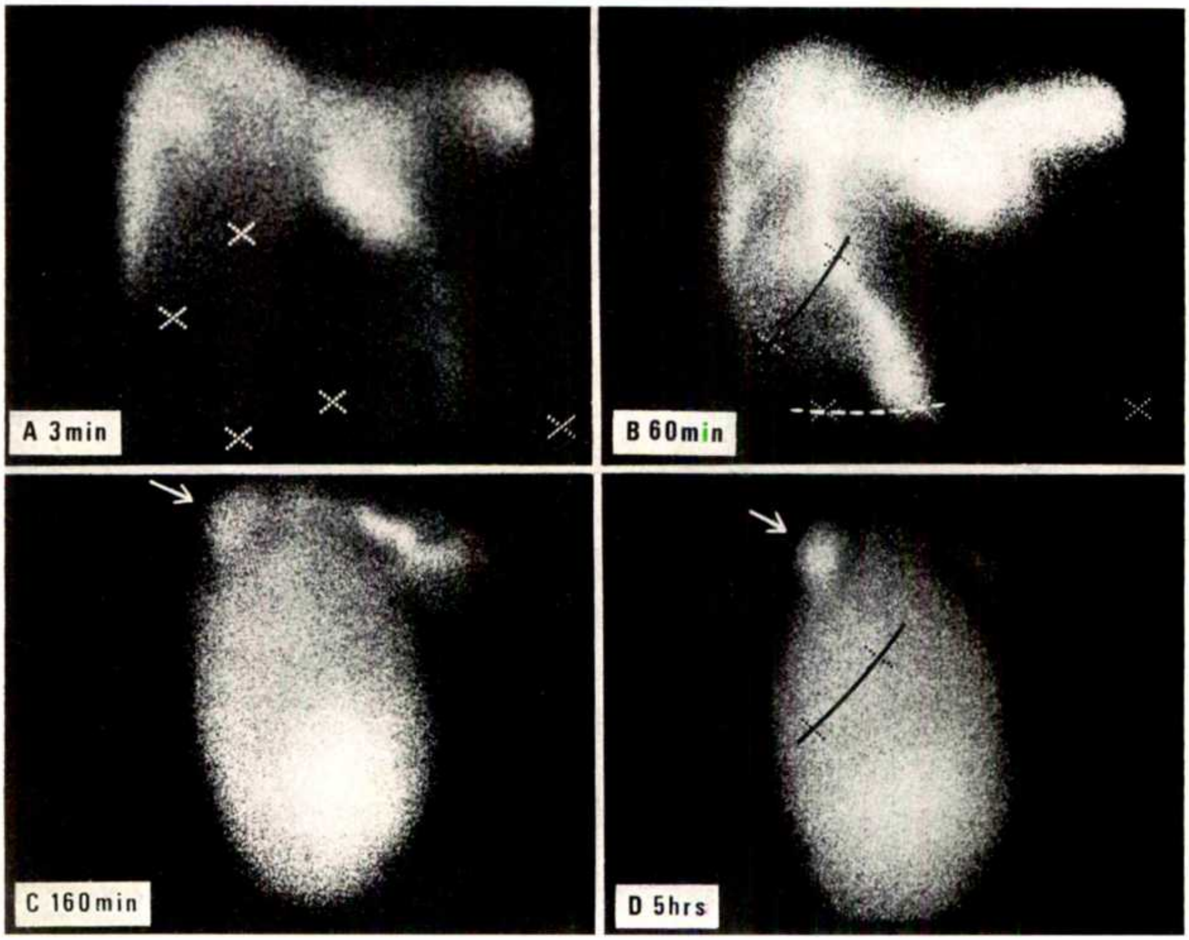


FIG. 2. *Case 2.*

Pre-operative $^{99}Tc^m$–EHIDA hepatobiliary scan. Filling defect in liver (A), filling of gall bladder and choledochal cyst (C, D).

course and a repeat $^{99}Tc^m$–EHIDA study revealed patency of the Roux-en-Y anastomosis. No bile leak or bile stasis in the anastomosed intestinal segment were seen. The tracer cleared promptly from the jejunal anastomosis.

DISCUSSION

Before the introduction of ^{131}I Rose Bengal hepatobiliary scintigraphy, choledochal cysts have rarely been correctly diagnosed pre-operatively. Delayed diagnosis is due to the fact that symptoms are nonspecific and intermittent and the classic triad is seldom seen. The short duration of such episodes and the negative work-up during remission often result in this condition being diagnosed as chronic or recurrent hepatitis or recurrent cholangitis or cholecystitis. Oral cholecystogram and intravenous cholangiogram are occasionally diagnostic in the non-jaundiced patient (Barlow *et al.*, 1976). Barium meal series is not diagnostic. Ultrasonogram demonstrates the presence of a cyst but is not always diagnostic and may be interpreted as an hepatic cyst.

Technetium 99m-diethyl-IDA has been shown to be the best for imaging of the hepatobiliary tract (Wistow *et al.*, 1977; Pauwels *et al.*, 1978). The finding on the scintiscan of an initial filling defect in the liver together with an area of no radioactivity over the palpable abdominal mass that becomes an area of concentration on the serial scan is pathognomonic for the disorder. In the non-jaundiced patient, filling of the cyst by the radionuclide can occur as early as two hours, whereas in the jaundiced patient filling may not be seen until the 24-hour scan.

The post-operative scans show loss of the filling defect and the prompt excretion of the tracer into the gut through the biliary anastomosis. Technetium 99m-diethyl-IDA scintigraphy also allows the assessment of the patency of the surgical biliary

1981, *British Journal of Radiology*, *54*, 1107–1109 DECEMBER 1981

anastomosis. Bile drainage along the Roux-en-Y anastomosis can be visualized and bile stasis in the anastomosed intestinal segment or bile leak can be demonstrated. This procedure is safe, sensitive and diagnostic, the findings being pathognomonic for choledochal cyst. It is the authors' opinion that ^{99}Tc^{m}-diethyl-IDA (EHIDA) hepatobiliary imaging should be the initial diagnostic procedure and may perhaps be the only one necessary where there is clinical suspicion of choledochal cyst.

ACKNOWLEDGMENTS

We would like to thank Miss Low for her secretarial assistance and the Medical Illustration Department for the illustrations.

REFERENCES

ALONSO-LEJ, F., REVER, W. B. and PESSAGNIO, D. J., 1959. Congenital choledochal cyst, with a report of two and an analysis of 49 cases. *Surgery, Gynecology and Obstetrics*, *108*, 1.

BARLOW, B., TABOR, E., BLANC, W. A., SANTULLI, T. V. and HARRIS, R. C., 1976. Choledochal cyst: A review of 19 cases. *Journal of Pediatrics*, *89*, 934–940.

HAN, S. Y., COLLINS, L. C. and WRIGHT, R. M., 1969. Choledochal cyst: report of five cases. *Clinical Radiology*, *20*, 332–336.

HARVEY, E., LOBERG, M. and COOPER, M., 1975. Tc-99m-HIDA: a new radiopharmaceutical for hepatobiliary imaging. *Journal of Nuclear Medicine*, *16*, 533.

PAUWELS, S., STEELS, M., PIRET, L. and BECKERS, C., 1978. Clinical evaluation of Tc-99m-diethyl-IDA in hepatobiliary disorders. *Journal of Nuclear Medicine*, *19*, 783–788.

WISTOW, B. W., SUBRAMANIAN, G., HEERTUM, R. L., HENDERSON, R. W., GAGNE, G. M., HALL, R. C. and MCAFEE, J. G., 1977. An evaluation of ^{99m}Tc- labelled hepatobiliary agent. *Journal of Nuclear Medicine*, *18*, 455–461.

WILLIAMS, L. E., FISHER, J. H., COURTNEY, B. A., and DARLING, D. B., 1970. Preoperative diagnosis of choledochal cyst by hepatoscintigraphy. *New England Journal of Medicine*, *283*, 85–86.

VATER, A., 1748. Dissertatio anatomica qua novum bilis diverticulum circa orificum ductus cholidochi. *Disputationum Anatomicarum Selectarum*, *3*, 259–273.

Cerebral nocardiosis in renal transplant patients

By *E. Barmeir, M.D., *J. H. Mann, M.B., B.Ch. and †R. H. Marcus, M.B., B.Ch.

Departments of *Diagnostic Radiology and †Nephrology, Johannesburg Hospital and University of the Witwatersrand, Jubilee Road, Parktown, Johannesburg 2193, South Africa

(*Received June 1981*)

Nocardiosis is a disease found with increasing frequency in both normal and compromised hosts (Curry, 1980). The organism is a gram positive acid-fast bacterium of the genus aerobic *Actinomycetacae*. Nocardiosis has been described in association with neoplastic disease (Young *et al.*, 1971), heart transplantation (Krick *et al.*, 1975), and renal transplantation as well as in the normal population (Weed *et al.*, 1955; Beaman *et al.*, 1976). When confined to the lungs, with appropriate antibiotic treatment, the survival rate may approach 75% (Palmer *et al.*, 1974). However, when cerebral involvement is present, the prognosis is poor with a mortality rate approaching 87% (Cupp *et al.*, 1960; Hoeprich *et al.*, 1968).

CASE REPORTS

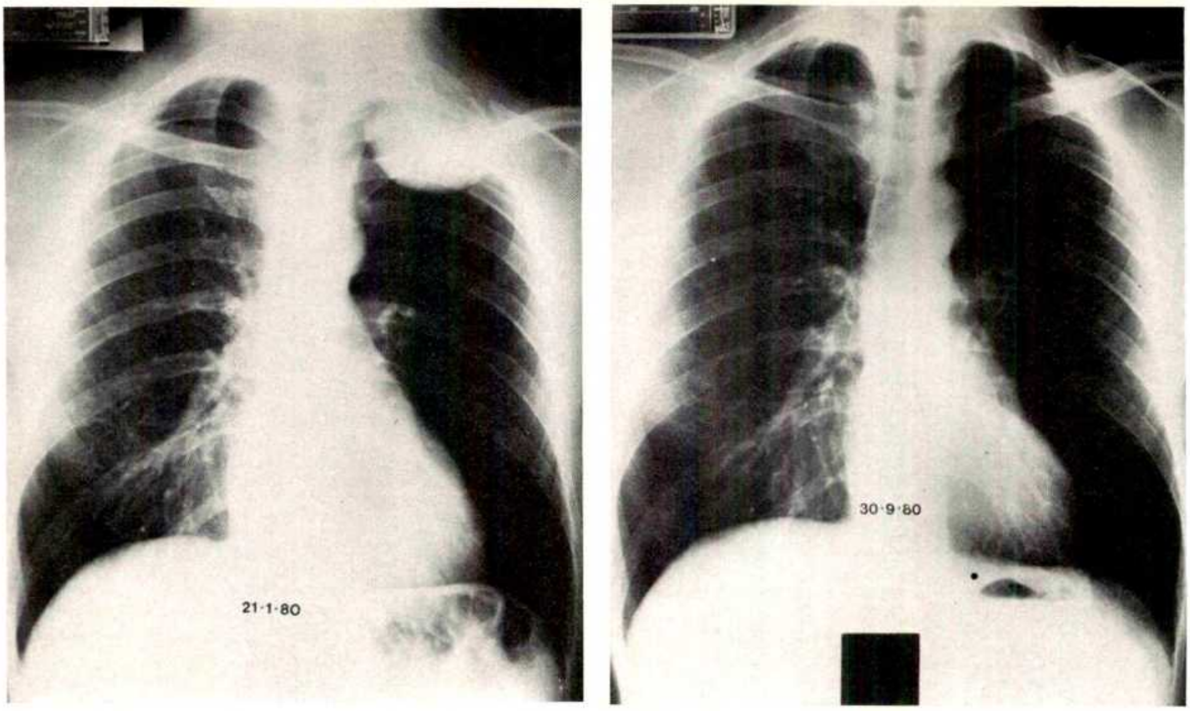
Case 1

A 35-year-old white male underwent cadaver donor renal transplantation three years ago. Two years later, while still on immunosuppressant therapy, he developed back pain, malaise and subcutaneous nodules. Chest radiograph showed a left-sided lesion with pleural–extrapleural configuration eroding bone (Fig. 1A) and nocardiosis was diagnosed histologically following a biopsy. The lesion was treated with combination therapy using Minocycline and Bactrim and resolved completely by September, 1980 (Fig. 1B). The patient remained well for the following six months but then represented with headache. Neurological examination was normal. CT scan on March 31, 1981 revealed a right temporal low-density area with smooth ring enhancement after intravenous contrast medium (Fig. 2). The abscess was drained surgically and *Nocardia* were demonstrated microscopically and on culture. The patient died as a result of surgical complications.

Case 2

A 45-year-old white male underwent related living-donor renal transplantation 14 months ago. Five months later, while still receiving immunosuppressant therapy, he developed cough, dyspnoea and a subcutaneous nodule in the left leg. Chest radiograph then revealed consolidation of the left lower lobe, a left hilar mass and pleural effusion. Nocardiosis was diagnosed histologically and for the following nine months the infection was treated with a combination of Minocycline and Bactrim as well as monthly Amikacin pulses. On this admission he presented with Jacksonian motor seizures of the facial muscles and right hand. CT scan revealed multiple low density areas with ring enhancement after intravenous contrast medium (Fig. 3). Because of the multiplicity of the cerebral abscesses, surgical drainage was not possible; medical treatment was continued. The patient is still alive three months after the diagnosis of the cerebral abscesses.

Requests for reprints: Dr. J. H. Mann.



A FIG. 1. *Case 1.* B

Regression of nocardial chest lesion with antibiotic treatment.

(A) Left apical mass with pleural–extrapleural configuration and rib erosion.

(B) A chest radiograph eight months later shows complete resolution of the mass and reconstitution of the rib.

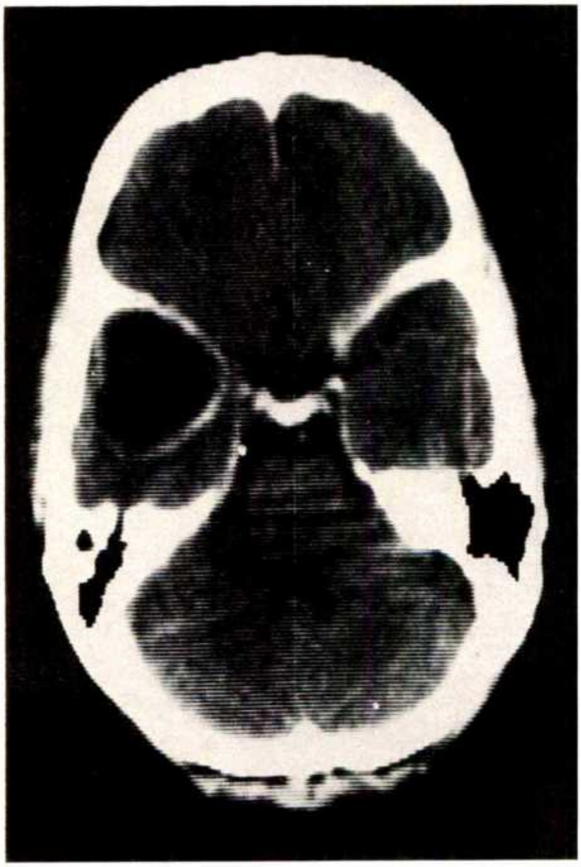


FIG. 2. *Case 1.*

Cranial CT scan after contrast medium showing a large ring enhancing lesion in the right temporal region.

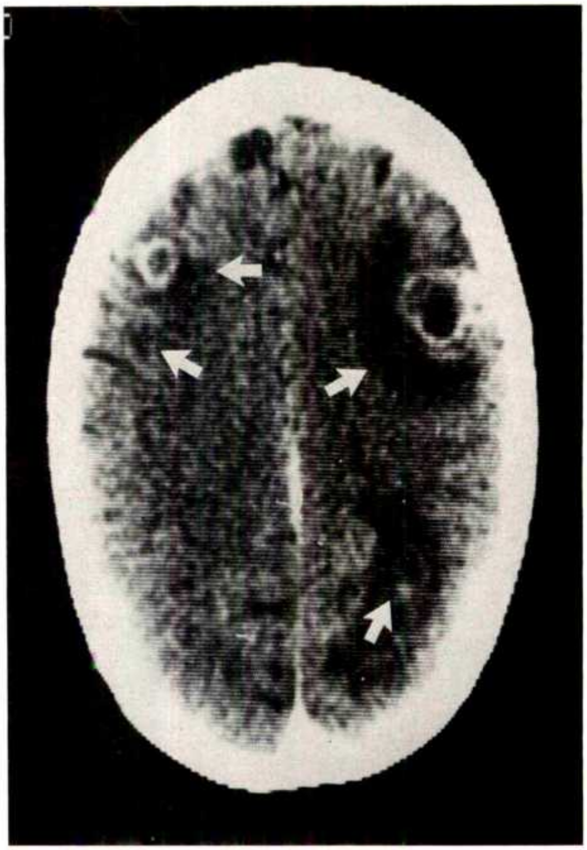


FIG. 3. *Case 2.*

Cranial CT scan after contrast medium demonstrating multiple ring enhancing lesions surrounded by vasogenic oedema (arrows).

1981, *British Journal of Radiology*, *54*, 1109–1111 DECEMBER 1981

DISCUSSION

Pulmonary nocardiosis has been described as the commonest primary site of involvement (73–77%) (Palmer *et al.*, 1974). The most common secondary site of involvement is the central nervous system which is associated with an extremely high mortality rate. In a review of 50 cases of cerebral nocardiosis from 1948 to 1970, Viroslav and Williams (1971) found only nine survivors.

The most appropriate therapy today is thought to be with sulphonamides or, in allergic patients or where resistance to sulphonamides is demonstrated, with Minocycline (Curry, 1980). Drainage of cerebral abscesses should be undertaken if surgically feasible. As the signs and symptoms of the disease are varied and non-specific, they often resemble those of other, more common diseases. The treatment of the latter differs from that of nocardiosis and, therefore, it is essential to establish an early, firm diagnosis. Nocardiosis should be considered in any immunosuppressed patient with the combination of a pulmonary lesion and cerebral symptoms. Aggressive combined medical and surgical treatment should be instituted early.

Radiographic evidence of improvement may be demonstrated on chest radiographs. However, in Case 1, in spite of disappearance of the pleuronocardiosis and the resolution of the associated rib lesion (Fig. 1B), dissemination occurred six months later.

In the second case systemic dissemination was demonstrated (Fig. 3), but due to the presence of multiple cerebral abscesses he was treated conservatively. There are only two previous reports of patients that have survived with nocardial brain abscesses on medical treatment alone (Viroslav and Williams, 1971; Kirmani *et al.*, 1978).

With the increased use of corticosteroids and immunosuppressive agents in organ transplant patients, nocardiosis is becoming a more common cause of cerebral disease. Early referral of these patients for cranial CT and radiological awareness of the diagnosis are necessary for correct identification of the characteristic areas of cerebritis and abscess formation.

ACKNOWLEDGMENT

We thank Professor A. M. Meyers for his invaluable assistance and advice.

REFERENCES

BEAMAN, B. L., BURNSIDE, J. and EDWARDS, B., 1976. Nocardial infections in the United States, 1972–1974. *Journal of Infective Deseases*, *134*, 286–289.

CUPP, D. M., EDWARDS, W. M. and CLEVE, E. A., 1960. Nocardiosis of the central nervous system. Report of two fatal cases. *Annals of Internal Medicine*, *52*, 223–229.

CURRY, W. A., 1980. Human nocardiosis: a clinical review with selected case reports. *Archives of Internal Medicine*, *140*, 818–826.

HOEPRICH, P. D., BRANDT, D. and PARKER, R. H., 1968. Nocardial brain abscess cured with Cycloserine and sulfonamides. *American Journal of Medical Science*, *255*, 208–216.

KIRMANI, N., TUAZON, C. U., OCUIN, J. A., THOMPSON, A. M., KRAMER, N. C. and GEELHOED, G. W., 1978. Extensive cerebral nocardiosis cured with antibiotic therapy alone. *Journal of Neurosurgery*, *49*, 924–928.

KRICK, J. A., STINSON, E. B. and Remington, J. S., 1975. Nocardia infection in heart transplant patient. *Annals of Internal Medicine*, *82*, 18–26.

PALMER, D. L., HAREY, R. L. and WHEELER, J. K., 1974. Diagnostic and therapeutic considerations in Nocardia asteroides infection. *Medicine*, *53*, 391–401.

VIROSLAV, J. and WILLIAMS, T. W., JR., 1971. Nocardial infection of the pulmonary and central nervous system: successful treatment with medical therapy. *South African Medical Journal*, 64, 1382–1385.

WEED, L. A., ANDERSON, H. A., GOOD, C. A. and BAGGENSTOSS, A. H., 1955. Nocardiosis: clinical, bacteriologic and pathological aspects. *New England Journal of Medicine*, *253*, 1137–1143.

YOUNG, L. S., ARMSTRONG, D. and BLEVINS, A., 1971. Nocardia asteroides infection complicating neoplastic disease. *American Journal of Medicine*, *50*, 269–276.

A case of aneurysm of the splenic artery visualized by dynamic ultrasonography

By L. Bolondi, M.D., P. Casanova, M.D., V. Arienti, M.D., S. Testa, M.D., S. Gaiani and G. Labò, M.D.

Department of Medicine, University of Bologna, Italy

(*Received May 1981*)

The possibility of using ultrasound to visualize the coeliac axis and its main branches, the splenic and common hepatic arteries, has already been extensively documented (Carlsen and Filly, 1976; Filly and Carlsen, 1976; Goldberg and Perlmutter, 1977; Skolnick and Royal, 1976). Using real time equipment we have identified a spherical echo-free space close to the origin of the splenic artery in a patient with undiagnosed abdominal pain. The ultrasound findings led us to suspect the presence of an aneurysm, which was subsequently confirmed, and surgical removal relieved the patient's symptoms. We are unaware of any other previous case report of a similar aneurysm diagnosed by ultrasound, with the exception of a mycotic aneurysm of the hepatic artery (Sukerkar, 1977). Without wishing to detract from the decisive role of angiography in such cases we would like to emphasize the important contribution real time ultrasonography can sometimes make in the diagnosis of disorders involving small calibre abdominal vessels.

CASE REPORT

A 41-year-old patient presented in December 1979 complaining of continuous central abdominal pain which was unrelated to meals but associated with indigestion, occasional vomiting and loss of weight. The patient had a previous hospital admission for gastro-duodenoscopy when a duodenal ulcer was diagnosed and subsequently treated with cimetidin and antacids. In our hospital an endoscopic examination was repeated and revealed the healed lesion. In addition gastric dyskinesia and pyloric incompetence with impaired gastric emptying were noted.

An ultrasound examination was performed to exclude possible disease involving the liver, bile-ducts and pancreas. The findings in these structures were essentially normal but a roundish transonic structure approximately 2 cm in diameter was identified posterior to the left lobe of the liver, anterior to the aorta and apparently related to the proximal portion of the splenic artery (Fig. 1, 2A, B). Although we had not previously seen a similar case, careful examination of the surrounding structures demonstrated direct continuity between the spherical lesion and the splenic artery. As a result of these findings, we established a provisional diagnosis of splenic artery aneurysm. Subsequent coeliac arteriography confirmed the ultrasound diagnosis (Fig. 3). The patient underwent surgery during which the aneurysm was found to be the size of a hazel-nut and was ligated both proximally and distally. Ten months after the operation the patient's symptoms showed considerable improvement.

DISCUSSION

Ultrasound examination usually allows visualization of the coeliac trunk at its point of origin from the anterior wall of the aorta, a few millimetres superior to the origin of the superior mesenteric artery. Its anterior course can also be followed up to its division into the common hepatic, splenic and gastric arteries. Whilst the latter vessel is usually difficult to identify, the bifurcation into common hepatic and splenic is normally displayed on transverse scans as a typical "seagull's wings", "fountain jet" or "Y-shaped" image. The hepatic artery then

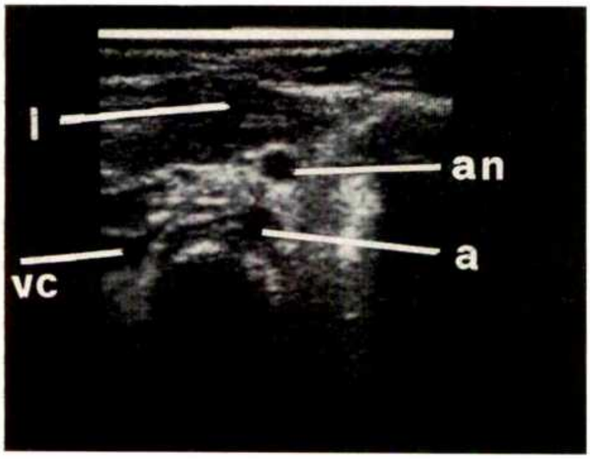


FIG. 1.

Transverse scan. The aneurysm (an) appears as a round transonic area anterior to the aorta and posterior to the left lobe of the liver. l = liver, a = aorta, vc = vena cava.

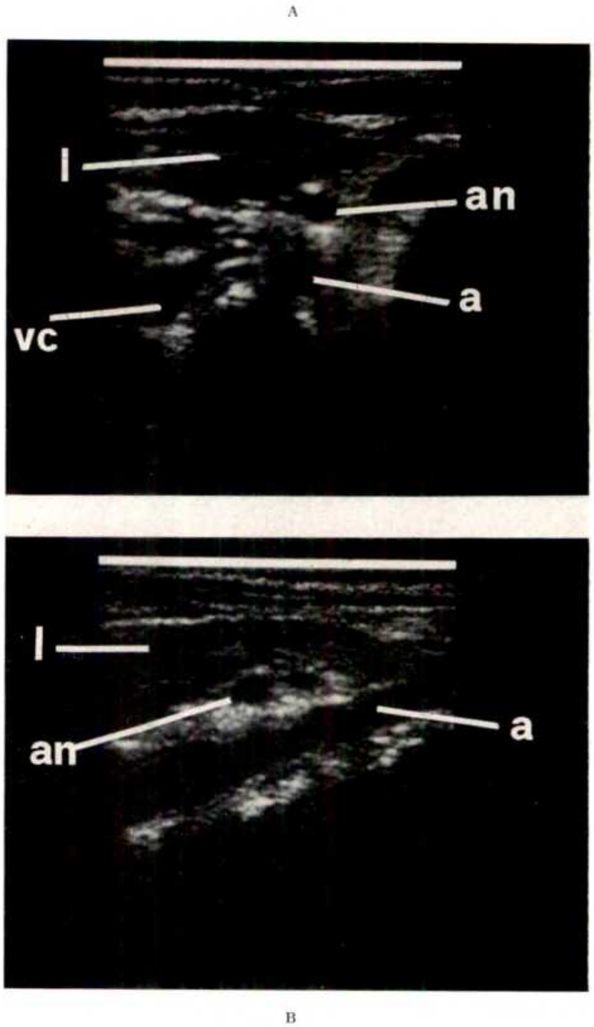


FIG. 2.

(A) Transverse scan. (B) Longitudinal scan. an = aneurysm of the splenic artery, a = aorta, l = liver, vc = vena cava.

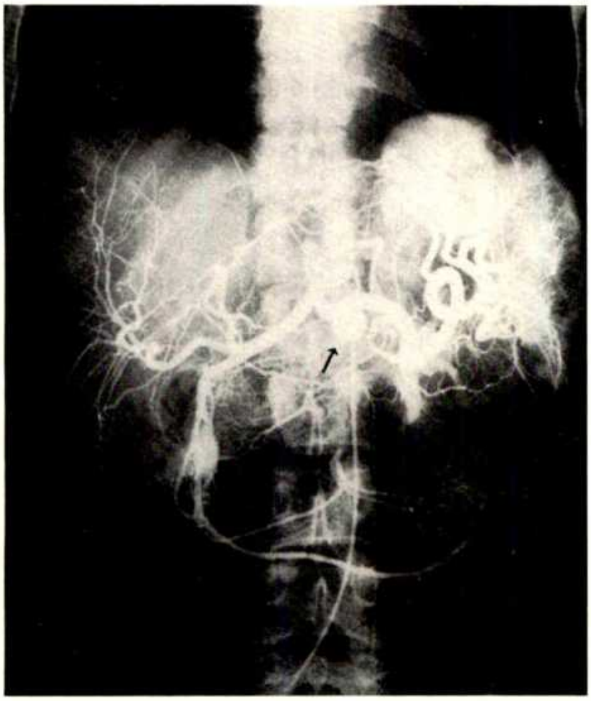


FIG. 3.

Selective arteriogram of the coeliac trunk. The aneurysm can be seen (arrowed) close to the origin of the splenic artery.

proceeds towards the right following the splenoportal axis, whilst the splenic artery courses to the left in relation to the posterior and superior parts of the body and tail of the pancreas. In the absence of intestinal meteorism, it is now possible to follow long stretches of these vessels with real time imaging.

The most common diseases displayed by ultrasound as a transonic area close to the origin of the splenic artery were considered in the differential diagnosis of this case. Thus after a careful study of the relations between this area and adjacent organs we were first able to exclude the possibility of a small pancreatic cyst, followed by a segmental dilatation of Wirsung's duct, ectasia of the splenic vein, lymphadenopathy or gastric varices. However, the conclusive evidence in favour of aneurysm was visualization of the continuity between the mass and the splenic artery.

In conclusion we would stress that dynamic ultrasonography not only makes it easier to identify small vascular structures in the upper abdomen, thereby supplying accurate reference points for correctly identifying other organs (Weill *et al.*, 1977), but may also be of diagnostic help in diseases involving these vessels.

ACKNOWLEDGMENT

The authors are grateful to Anne Collins for translating the manuscript.

REFERENCES

CARLSEN, E. N. and FILLY, R. A., 1976. Newer ultrasonographic anatomy in the upper abdomen. I. The portal and hepatic venous anatomy. *Journal of Clinical Ultrasound*, *4*, 85–90.

FILLY, R. A. and CARLSEN, E. N., 1976. Newer ultrasonographic anatomy in the upper abdomen. II. The major systemic veins and arteries with a special note on localization of the pancreas. *Journal of Clinical Ultrasound*, *4*, 91–96.

GOLDBERG, B. B. and PERLMUTTEF, G., 1977. Ultrasonic evaluation of the superior mesenteric artery. *Journal of Clinical Ultrasound*, *5*, 185–187.

SKOLNICK, M. L. and ROYAL, D. R., 1976. Normal upper abdominal vasculature: a study correlating contact B scanning with arteriography and gross anatomy. *Journal of Clinical Ultrasound*, *4*, 399–402.

SUKERKAR, A. N., DULAY, C. C., ANAUDAPPA, E. and ASOKAN, S., 1977. Mycotic aneurysm of the hepatic artery. Case diagnosed with radionuclide imaging and ultrasound. *Radiology*, *124*. 444.

WEILL, F., SCHRAUB, A. and EISENSCHER, A., 1977. Ultrasonography of the normal pancreas. *Radiology*, *123*, 417–423.

Book review

Radiation Protection. Ion Chambers for Neutron Dosimetry. Ed. by J. J. Broerse, pp. 350, 1980 (Harwood, London), $57.00.

ISBN 3-7186-0048-A

This monograph is based on a workshop held during September 1979 in Rijswijk and has the stated aim of reviewing the current status of ion chambers and their use for neutron dosimetry. This it achieves well but suffers the disadvantages of any such collection of papers in that the presentations vary in quality and information is not always readily found and extracted. However, this is a very useful work and contains much information on ionization chambers and their operational characteristics not found elsewhere. Eight different chambers are discussed and review papers on kerma values, stopping power, $\overline{W}$ values and k_u, the relative neutron sensitivity of photon dosemeters, are presented. The book also includes detailed discussions of many practical aspects of ion chamber measurements. As a reference work it will be of most benefit to workers in the field, and would be profitably read by those about to engage in neutron dosimetry.

D. E. BONNETT.

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Moloney's line

THE EDITOR—SIR,

I can only presume that the absence of formal editing of letters allowed the communication by Drs. Karle and Hansen to be published in your journal (1981). The "new line" to which they refer is well-known by many skeletal radiologists and is usually referred to as Moloney's line. I cannot provide an original reference, but the line was attributed to Moloney by Dorgan (1955) and is mentioned in detail in a standard textbook on fractures (Rockwood and Green, 1975). It cannot, therefore, be regarded as new, but perhaps some useful purpose will have been achieved by your correspondents' letter, as ignorance of this line and its value may be greater than I had supposed. I should perhaps express the hope that the transthoracic view of the shoulder joint is nowadays being used very infrequently.

Yours, etc.,
D. J. STOKER.

The Institute of Orthopaedics,
Royal National Orthopaedic Hospital,
234 Great Portland Street,
London W1N 6AD
(*Received August 1981*)

REFERENCES

DORGAN, J. A., 1955. Posterior dislocation of the shoulder. *American Journal of Surgery*, *89*, 890–900.

KARLE, A. and HANSEN, E. B., 1981. A "new line "in radiology. *British Journal of Radiology*, *54*, 691–693.

ROCKWOOD, C. A. and GREEN, D. P., 1975. *Fractures* (J. P. Lippincott, Philadelphia), p. 705.

(*Note by Honorary Editor:* Dr. Stoker may rest assured that formal editing of letters is invariably undertaken and the reasons for publication of Drs. Karle and Hansen's original letter have been correctly inferred in his penultimate sentence. His final sentence expresses a hope that we fully share.)

(*Authors' reply*)

THE EDITOR—SIR,

We thank Dr. Stoker for drawing our attention to the two references and notice that it is more than thirty years since Moloney described the same line in the shoulder joint on the transthoracic view alone.

When we first became aware of the line—on the frontal as well as on the transthoracic view, we did wonder why this line, principally so like Shenton's line, had not been described before. We are glad that attention has been drawn to Moloney who evidently is not well known to all radiologists. As to the transthoracic view, we consider it preferable to the tangential projection, which is more difficult to interpret, and to the axial projection, which is more unpleasant to injured patients.

Yours, etc.,
A. KARLE,
E. B. HANSEN.

Department of Radiology,
Hvidovre Hospital,
University Hospital of Copenhagen,
DK-2650 Hvidovre, Denmark.
(*Received September 1981*)

Thiol radioprotection *in vivo*: the critical role of tissue oxygen concentration

THE EDITOR—SIR,

Lunec *et al.* (1981) have recently pointed out that when exogenous free thiols are added to cells they have a marked radioprotective effect on cells at an intermediate radiosensitivity, and have less effect on aerobic radiosensitive cells or on hypoxic radioresistant cells. The oxygen concentration at which the maximum protection occurs corresponds to the *K* value for these cells. They caution that a considerable radioprotection of tumours, as was reported by Rojas and Stewart (1981), at low radiation doses might be expected if tumour cells are at such an intermediate oxygen tension.

We have recently extended our tumour studies to low single doses of radiation and to fractionated treatments, where cells at high to intermediate oxygen tensions should dominate the response. We have also studied the effects of varying oxygen concentration on the degree of radioprotection observed with the phosphorylated sulphydryl WR-2721 in normal mouse skin. Whilst the cautionary note struck by Lunec *et al.* (1981) is appropriate, our experimental data indicate that the critical oxygen tension at which maximum radioprotection is observed exists in normal tissues rather than in tumours.

Firstly, the large radioprotection (PF = 2.0) of a fibrosarcoma that was reported by Rojas and Stewart (1981) at low radiation doses has not been observed in subsequent experiments on the same tumour. Much smaller protection factors (1.0–1.3) have been observed, even at low doses (Rojas and Stewart, in preparation). In a different tumour, the mammary carcinoma NT, similar small protection factors (1.1–1.4) have been observed both with single doses and with two and five daily fractions, when reoxygenation is known to occur (Rojas and Denekamp, in preparation). The presence of marginally hypoxic cells in these tumours does not appear to lead to any marked radioprotection.

Secondly, in skin reaction experiments on the foot of unanaesthetized mice, the radioprotection with 400 mg/kg WR-2721 is significantly greater in animals irradiated in air (1.5) than in those irradiated in oxygen (1.2) (Stewart and Rojas, 1982).

Finally, we have used the Withers epidermal clone system to look at the influence of a wide range of inhaled oxygen concentrations on the radioprotection achieved with WR-2721 (Withers, 1967). Some of the data from these experiments are illustrated in Fig. 1. Animals were irradiated with 0.86 MeV electrons from a Van de Graaff generator, at a dose rate of 100 Gy (10 krad) per minute. The animals were exposed to the stated oxygen concentrations for 35–60 s before irradiation. It has previously been shown that 20 s in nitrogen gives full radioprotection (Denekamp *et al*, 1974). WR-2721 was administered IP as a fresh solution in distilled water 45–60 min before irradiation. Two things are apparent from Fig. 1. The skin of mice irradiated without the WR-2721 (open circles) becomes progressively more resistant as the oxygen content is decreased from 100% to 0%, indicating that some loss of sensitivity occurs even with air or 10% oxygen. Secondly, the radioprotection by WR-2721 is highest in air-breathing mice and is lower in mice breathing either 100% oxygen or 10% oxygen. There is virtually no protection in nitrogen.

These data, together with others from the same experiments, are summarized in Fig. 2. The oxygen enhancement ratio has been plotted as a function of the oxygen content of the inhaled gas. The OER has been calculated as the ratio of the dose needed in 100% nitrogen without drug to that needed

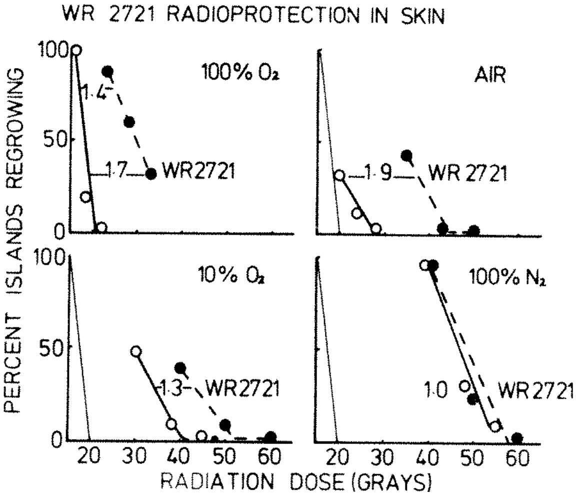


FIG. 1.

The survival of epidermal clones after irradiation of mice breathing different gases. The response to radiation alone (○) shows a progressive resistance as the oxygen concentration is reduced from 100%. The oxygen line is reproduced in each panel (without points) for comparison. The radioprotection observed with 400 mg/kg WR-2721 (●) is maximal in air, being smaller in 100% or 10% oxygen and non-existent in nitrogen.

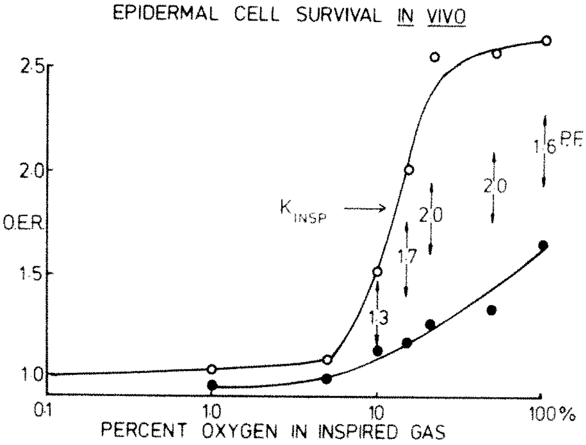


FIG. 2.

The oxygen enhancement ratio as a function of oxygen concentration in the inspired gas. The "K_{insp}" occurs at 13% oxygen. The protection factors for WR-2721 are indicated against each pair of points. The maximum sulphydryl protection occurs in air and 50% oxygen. ○, radiation alone. ●, with 400 mg/kg WR-2721.

in the relevant gas phase to give the same proportion of islands regrowing. The inspired gas that gives half the full oxygen effect (which we have called "K_{insp}") is 13% oxygen. The maximum radioprotection is seen just above the transition region from fully sensitive to fully resistant; this might be expected if the oxygen supply is then barely adequate and the sulphydryls and oxygen are competing for fixation and repair of damage. The *in vitro* data from Cullen *et al.* (1980) showed a displacement of the oxygen *K* curves when the sulphydryl dithioerythritol was added, but it occurred at a 40-fold lower oxygen concentration in the bubbled gas than in the inspired gas *in vivo*. Of course the "K_{insp}" value gives no direct information about the local oxygen tension at the critical site within the epidermal cells, so these data cannot be directly related to the *K* values *in vitro*.

We have considered the possibility that the high oxygen concentration "K_{insp}" in skin could be an artefact associated with anaesthesia, method of restraint or induced hypoxia resulting from the high dose-rate. A dose-rate-induced hypoxia was reported by Hornsey (1970) for intestine irradiated at 60 Gy/min but was not observed in skin irradiated at 700 Gy/min (Field and Bewley, 1974). We have investigated the effect of nembutal anaesthesia and found it does not protect mouse skin. We have also repeated the clone experiments, using low dose-rate X rays (3 Gy/min) on unanaesthetized, minimally restrained mice, and have seen no evidence of induced hypoxia in the electron-treated mice.

The data presented here confirm that, *in vivo*, the precise oxygen concentration in tissues strongly influences the radioprotection achieved with sulphydryl compounds, and the maximum effect occurs in the transition region from hypoxic to oxic sensitivity. However, many normal tissues may already be much closer to the transition between oxic sensitivity and hypoxic radioresistance than is generally appreciated, as was suggested by Hendry (1979). This is implicit in the use of 5–7% oxygen to make bone marrow, gut and oesophagus radioresistant (*e.g.* Phillips and Ainsworth, 1969; Phillips, 1969; Hornsey, 1972) but has not been demonstrated so clearly before.

We believe these results have an important bearing on the role of both sulphydryl radioprotectors and electron-affinic radiosensitizers in influencing normal tissue damage from radiation.

Yours etc.,
J. DENEKAMP,
B. D. MICHAEL,
A. ROJAS,
F. A. STEWART.

Gray Laboratory,
Mount Vernon Hospital,
Northwood,
Middlesex HA6 2RN

REFERENCES

CULLEN, B. M., MICHALOWSKI, A. and WALKER, H. C., 1980. Correlation between the radiobiological oxygen constant, K, and the non-protein sulphydryl content of mammalian cells. *International Journal of Radiation Biology*, *38*, 525–535.

DENEKAMP, J., MICHAEL, B. D. and HARRIS, S. R., 1974. Hypoxic cell-radiosensitizers: comparative tests of some electron affinic compounds using epidermal cell survival *in vivo*. *Radiation Research*, *60*, 119–132.

FIELD, S. B. and BEWLEY, D. K., 1974. Effects of dose-rate on the radiation response of rat skin. *International Journal of Radiation Biology*, *26*, 259–267.

HENDRY, J. H., 1979. Quantitation of the radiotherapeutic importance of naturally hypoxic normal tissues from collated experiments with rodents using single doses. *International Journal of Radiation Oncology, Biology, Physics*, *5*, 971–976.

HORNSEY, S., 1970. The effect of hypoxia on the sensitivity of the epithelial cells of the jejunum. *International Journal of Radiation Biology*, *18*, 539–546.

1972. Sensitization of hypoxic cells *in vitro* with triacetoneamine N-oxyl (TAN). *International Journal of Radiation Biology*, *22*, 91–94.

LUNEC, J., CULLEN, B. M., WALKER, H. and HORNSEY, S., 1981. A cautionary note on the use of thiol compounds to

1981, *British Journal of Radiology*, 54, 1114–1115

protect normal tissues in radiotherapy. *British Journal of Radiology*, *54*, 428–429.
Phillips, T. L., 1969. Discussion after late effects on vascular tissue. In *Time and Dose Relationships in Radiation Biology as Applied to Radiotherapy* (Brookhaven National Laboratory 50203 (C-57)), pp. 194–199.
Phillips, T. L. and Ainsworth, E. J., 1969. Altered split-dose recovery in mice irradiated under hypoxic conditions. *Radiation Research*, *39*, 317–331.
Rojas, A. and Stewart, F. A., 1981. Radioprotection by WR-2721 in normal mouse skin and tumour (Abstract). *British Journal of Radiology*, *54*, 368.
Stewart, F. A. and Rojas, A., 1982. Radioprotection of mouse skin by WR-2721 in single and fractionated treatments. *British Journal of Radiology*, *55* (in press).
Withers, H. R., 1967. The dose survival relationship for irradiation of epithelial cells of mouse skin. *British Journal of Radiology*, *40*, 187–194.

Modification of gallium 67 citrate distribution in man following the administration of iron

The Editor—Sir,

Smith and Dendy (1981) suggest that the intramuscular injection of an iron-sorbital citrate complex two hours before the intravenous administration of carrier-free ^{67}Ga citrate "enhances the lesion-to-background ratio and makes earlier imaging and diagnosis possible". We would suggest that neither the evidence they provide in their paper, nor the references they quote, justify these conclusions for the following reasons:

(1) Their observations are uncontrolled except by "previous experience in this hospital". No data is given to indicate that any attempt was made to match even against historical controls, and no statistical support is given for their conclusions.

(2) The probable mechanism of localisation of gallium in tumours requires gallium to be bound to transferrin (Larson, 1978). Iron displaces gallium from transferrin (Hara, 1974) and is therefore likely to reduce tumour uptake and accelerate excretion. This was confirmed by Turner *et al.* (1979) who found that gallium uptake by mouse melanoma cells decreased as the iron content of the culture fluid was increased. Hammersley and Taylor (1980) did indeed find that iron reduced soft-tissue levels of ^{67}Ga in mice, but significantly the tumour to normal tissue ratios were unchanged for most tumours.

(3) Sephton and Martin (1980) gave iron about 3 h after the gallium with the intention of accelerating the excretion of circulating gallium. They found lower plasma levels of ^{67}Ga than in untreated patients but were unable to demonstrate that this affected diagnostic accuracy. Giving the iron before the gallium is unlikely to improve the ratio. As Smith and Dendy have measured neither plasma gallium, plasma iron nor TIBC they are unjustified in coming to any conclusions from their data.

(4) The authors appear to have misunderstood the paper by Sephton and De Abrew (1979). The latter administered desferroxamine, a chelating agent which accelerates the excretion of trivalent cations. By administering this agent after the gallium they hoped to increase the excretion of gallium still circulating after uptake had occurred into tumour. In practice they found it had little effect on tumour-to-background ratios. Similarly unpromising results were obtained by Hurwitz *et al.* (1975) using EDTA. This suggests that "tumour bound gallium" is still exchangeable with circulating gallium. If this is indeed the case, other early manipulations of circulating gallium levels are unlikely to have more than a marginal or transitory effect.

(5) The effect of carrier quantities of certain trivalent cations (ferric iron, scandium, indium, gallium) on the distribution of gallium and other group III metals has been known for many years (Bruner *et al.*, 1953), and was at one time used to obtain bone scans with gallium. There is a striking similarity between the authors' figures and those of Hayes *et al.* (1965), which the latter interpreted as evidence that in the presence of carrier gallium acts as a bone scanning agent (although neither the present nor the previous authors actually measured tissue levels of radioactivity)! The effect of pretreatment with iron was first noted by Wright (1970) with indium, although the significance of this observation was not fully appreciated at the time (Merrick, 1975).

(6) There are considerable variations between individual patients in the rate of excretion of gallium (Watson *et al.*, 1973). No data have been published on the range of variation to be found between the faecal and urinary routes or the factors which influence this. *A priori* iron saturation of transferrin is likely to be one of the determinants. In view of the extremely high specific activities of commercially available ^{67}Ga no consistent effect would be expected until TIBC is fully saturated.

There are therefore considerable theoretical grounds and much experimental evidence to doubt that iron will appreciably improve the tumour-to-background ratios with gallium. The anecdotal data provided by Smith and Dendy in no way alter this conclusion, and do not justify the administration of a drug which is not entirely free of the risk of serious side-effects.

Yours, etc.,
F. A. M. Doull,
M. V. Merrick.

Western General Hospital,
Crewe Road,
Edinburgh EH4 2XU.

(*Received July 1981*)

REFERENCES

Bruner, H. D., Hayes, R. L. and Perkinson, J. D., 1953. A study of gallium 72X. Preliminary data on gallium-67. *Radiology*, *61*, 534–613.
Hammersley, P. A. G. and Taylor, D. M., 1980. The effect of the administration of iron on gallium 67 citrate uptake in tumours. *British Journal of Radiology*, *53*, 563–571.
Hara, T., 1974. On the binding of gallium to transferrin. *Journal of Nuclear Medicine and Biology*, *1*, 152–154.
Hayes, R. L., Carlton, J. E. and Byrd, B. L., 1965. Bone scanning with gallium 68: a carrier effect. *Journal of Nuclear Medicine*, *6*, 605–610.
Hurwitz, S. R., Hagan, P. L. and Alazraki, N. P., 1975. Distribution of ^{67}Ga following intravenous administration: effects of disodium acetate therapy. *Journal of Nuclear Medicine*, *16*, 280–283.
Larson, S. M., 1978. Mechanisms of localisation of gallium-67 in tumours. *Seminars in Nuclear Medicine*, *8*, 193–203.
Merrick, M. V., 1975. Review article: bone scanning. *British Journal of Radiology*, *48*, 327–351.
Sephton, R. and Martin, J. J., 1980. Modification of distribution of gallium 67 in man by administration of iron. *British Journal of Radiology*, *53*, 572–575.
Sephton, R. and De Abrew, S., 1979. Effects of desferroxamine on ^{67}Ga distribution in tumour bearing mice. *Proceedings of the Society for Experimental Biology and Medicine*, *161*, 402–406.
Smith, F. W. and Dendy, P. P., 1981. Modification of gallium-67 citrate distribution in man following the administration of iron. *British Journal of Radiology*, *54*, 398–402.
Turner, U. K., Wong, H., Noujaim, A. A., Lentle, B. C. and Hill, J. R., 1979. ^{67}Ga and ^{59}Fe uptake in human melanoma cells. *International Journal of Nuclear Medicine and Biology*, *6*, 23–28.

Watson, E. E., Cloutier, R. J. and Gibbs, W. D., 1973. Whole body retention of gallium citrate. *Journal of Nuclear Medicine*, *14*, 840–842.

Wright, F. W., 1970. Placental localisation by isotope scanning with ^{113m}In. Results in 200 patients. *British Medical Journal*, *i*, 636–639.

(*Authors' reply*)

The Editor—Sir,

The letter by Doull and Merrick on this subject is welcome because it draws attention to the complexity of the mechanism by which ^{67}Ga citrate concentrates selectively in many human tumours. However, we believe it is an unreasonable commentary on our work because it does not take into account the numerous pieces of evidence, many of which are to be found in the papers quoted by Doull and Merrick, supporting the action we have taken.

For example Larson (1978) certainly suggested that localisation of gallium in tumours requires gallium to be bound to transferrin but this observation was based largely on *in vitro* studies. In the same article he implied that the uptake mechanism might be different *in vivo* by quoting the work of Hayes (1976) who had already shown that, when scandium was administered to animals simultaneously with ^{67}Ga citrate, there was rapid clearance of ^{67}Ga from soft tissues but uptake into tumours was not greatly affected. Thus there was a relative improvement in the tumour/non-tumour tissue ratio. The effects of iron on ^{67}Ga uptake are very similar to those of scandium and in an abstract submitted to the International Symposium on Gallium & Related Elements (Banff Springs, September 1980) Sephton stated that "very few analogies with Fe are perceived in ^{67}Ga distributions *in vivo*—moreover the principal cell culture findings seem almost irrelevant in this context".

The latest paper from Hayes *et al.* (1981) shows that administration of IV iron citrate or IM imferon or IV scandium citrate will reduce gallium uptake into normal soft tissue but not into tumour. This is strong evidence that ^{67}Ga citrate binds to tumour by a mechanism which differs from that by which it binds to normal tissues, with transferrin binding being heavily involved in the latter but not in the former.

Hayes *et al.* (1981) propose a model involving reversible diffusion of ^{67}Ga into tumour but followed by irreversible binding. Sephton and De Abrew (1979) also concluded that ^{67}Ga was irreversibly bound to tumour by 24 h, and this is supported by our observations on a few patients scanned at 24, 48 and 72 h, where we have never seen appreciable loss of activity from tumour deposits.

Finally, Hayes *et al.* (1981) worked with the 5123C Morris hepatoma in rats, the only animal tumour to our knowledge that shows a degree of ^{67}Ga avidity comparable th that frequently observed in humans. Hammersley and Taylor (1980) used animal tumours which showed much less gallium avidity. Nevertheless, they did find small improvements in the tumour-to-soft tissue ratio for three of the four tumours at 4 h after iron treatment and commented that "the tumour levels of ^{67}Ga are relatively less affected by the administration of iron than are other tissue ^{67}Ga concentrations". Furthermore Hammersley and Taylor found that prior injection of iron generally gave the greatest effect. This also supports the protocol we have adopted.

Thus, contrary to the implications of the above letter, we maintain that there are well documented laboratory findings that *in vivo* uptake of ^{67}Ga can proceed efficiently in gallium-avid tumours even when ^{67}Ga transport by circulating transferrin has been largely abolished. If uptake of ^{67}Ga into normal tissues is inhibited by iron saturation, improved tumour/background ratios will ensue.

Turning to our own, ongoing, clinical experience,

1. A report based on 147 patients can hardly be called "anecdotal".
2. We have rejected as ethically unacceptable the most stringent trial, which would be to perform the gallium scan twice on the same patient, once with and once without Jectofer.
3. Under the circumstances, comparison with a previous series in our own hospital seems reasonable since the disease spectrum of patients referred for gallium scanning varies markedly from one centre to another and this can have a big effect on diagnostic accuracy. Statistical analysis would have implied a more rigid comparison than we consider justified at the present time.
4. Merrick and Doull omit to mention that we did take a blood sample from each of 36 patients in our preliminary study (Smith *et al.*, 1980) and made careful measurements of plasma iron, percentage iron saturation of plasma transferrin and ^{67}Ga clearance from the blood. It was not considered justified to take blood samples in the larger series.
5. The fifth point of the letter by Merrick and Doull seems irrelevant. All reports, including our own detailed studies on gallium distribution in animals (Pocklington, unpublished data), confirm that in the presence of excess iron there will be increased uptake of ^{67}Ga into the skeleton.
6. All patients are screened carefully for contra-indications to Jectofer which is not administered in doubtful cases. To date over 300 patients have been rendered hyperferraemic in this way with no adverse reactions.
7. A study is currently in progress of the urinary clearance of ^{67}Ga in patients who have received Jectofer.
8. Since introducing the Jectofer procedure, requests for ^{67}Ga scans have increased from 55 during the first six months of 1979 to 88 during the first 6 months of 1981, so our "customers", the referring clinicians, seem well satisfied with the accuracy of the service we are providing. The saving in time between the request for a ^{67}Ga examination and a report is also appreciated.

Yours, etc.,

F. W. Smith,
P. P. Dendy.

Department of Bio-Medical Physics and Bio-Engineering,
University of Aberdeen.

(*Received September 1981*)

REFERENCES

Hammersley, P. A. G. and Taylor, D. M., 1980. The effect of the administration of iron on gallium 67 citrate uptake in tumours. *British Journal of Radiology*, *53*, 563–571.

Hayes, R. L., 1976. Factors affecting uptake of radioactive agents by tumour and other tissues in tumour localisation with radioactive agents. IAEA-MG-50/14 (International Atomic Energy Agency, Vienna) p. 29.

Hayes, R. L., Rafter, J. J., Byrd, B. L. and Carlton, J. E., 1981. Studies of the in vivo entry of ^{67}Ga into normal and malignant tissue. *Journal of Nuclear Medicine*, *22*, 325–332.

Larson, S. M., 1978. Mechanisms of localisation of gallium-67 in tumours. *Seminars in Nuclear Medicine*, *8*, 193–203.

Sephton, R. and De Abrew, S., 1979. Effects of desferrioxamine on ^{67}Ga distribution in tumour bearing mice. *Proceedings of the Society for Experimental Biology and Medicine*, *161*, 402–406.

Smith, F. W., Dendy, P. P., Pocklington, T., Dawson, A. A., Foster, M. A. and Mallard, J. R., 1980. A preliminary investigation of ^{67}Ga citrate distribution in hyperferraemic patients. *European Journal of Nuclear Medicine*, *5*, 327–332.

1981, *British Journal of Radiology*, *54*, 1116

Correspondence

Use of ultrasound to measure the lumbar spinal canal

THE EDITOR—SIR,

After two-years' clinical experience with symptomatic and volunteer patients, I find I am in firm agreement with Stockdale and Finlay's (1980) original communication on this subject. Attempts in this department both at adherence to Porter's *et al.* (1978) original protocol and modifications of this have shown that in any given patient there is no unique "oblique sagittal" dimension to measure. The problem is compounded if the scanning position is changed to give optimal images. Further, the essentially mid-line "window" into the lumbar canal (the interlaminar space), due to lumbar lordosis, becomes further from the skin as one scans down the lumbar spine. Hence, angulation of the transducer toward the mid-line, and scanning along a line, say 1 cm away from but parallel to the mid-line, will result in measurements of the canal diameter being made progressively toward the opposite side. A narrow measurement at one level may therefore indicate a contralateral lesion. The not inconsiderable beam-width of typical transducers necessary to image the depths involved will also add uncertainty. A measurement may be reproducible (Ottewell and Howells, 1981) but may not, in fact, be clinically useful, or even necessarily a measurement of the anatomical site imagined.

Much of the spinal canal is in the acoustic shadow of laminae, and significant focal pathology will be missed as this cannot be interrogated by the examining beam. Finally, but related to the above problem, the interlaminar space narrows with age and it is often impossible to obtain satisfactory measurements through this "keyhole" in elderly, symptomatic patients. I believe that these difficulties and those referred to elsewhere indicate that this technique using present-day general-purpose equipment can have little place in the work-up of the symptomatic patient, and the investigation has been abandoned in this department.

Yours, etc.,
B. E. CHATTERTON.

Division of Nuclear Medicine,
Institute of Medical and Veterinary Science,
Ultrasound Service,
Royal Adelaide Hospital,
North Terrace,
Adelaide, South Australia 5000.
(*Received September 1981*)

REFERENCES

OTTEWELL, D. and HOWELLS, P., 1981. The use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *54*, 430.

PORTER, R. W., WICKS, M. and OTTEWELL, D., 1978. Measurement of the spinal canal by diagnostic ultrasound. *Journal of Bone and Joint Surgery*, *60B*, 481–484.

STOCKDALE, H. R. and FINLAY, D., 1980. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *53*, 1101–1102.

THE EDITOR—SIR,

The letter of Nachemson and Asztély (1981) is a useful contribution to the debate on ultrasound scanning of the lumbar spine.

Whether the "debate has lost its structure" is difficult for us to assess, but we do agree with the distinctions that they draw between the quality of the recorded values and their clinical usefulness. They are separate topics but one cannot appreciate the true role of this or any other diagnostic technique in clinical medicine without a realistic knowledge of artefacts. Our intentions are to highlight such artefacts so that potential users can put it in its true perspective.

We do not consider that the doubts expressed by various authors regarding the accuracy and reproducibility of the results will be satisfactorily settled by deducing the primary echo-generating interfaces. Of the echogenic interfaces in and around the lumbar neurocanal, we would expect that the bone/soft tissue interfaces will generate more intense echoes than cerebrospinal fluid/soft tissue boundaries. We need to see their results on autopsy specimens in print in order to comment correctly on their suggestion.

Regarding the present clinical usefulness of the technique, we concur with their scepticism on its use as a diagnostic agent in individual patient management.

The point made by Nachemson and Asztély on the subject of the epidemiological assessment of the different categories of spinal geometry is correct. If individuals can be separated into those with a narrow canal and those with a broad canal, then assuming that the subjective systematic errors do not significantly alter, the random errors associated with the measurements will tend to cancel out if sufficiently large numbers of individuals are studied in each group. Consequently, differences will be indicated between the groups but because of the presence of significant systematic errors, little faith can be placed in the absolute values recorded. The origins of these errors are discussed elsewhere (Finlay *et al.*, 1981).

Yours, etc.,
H. R. STOCKDALE,

Medical Physics Department,
City Hospital,
Nottingham NG5 1PB .

D. FINLAY.

X-ray Department,
Royal Infirmary,
Leicester.
(*Received September 1981*)

REFERENCES

FINLAY, D., STOCKDALE, H. R. and LEWIN, E., 1981. An appraisal of the use of diagnostic ultrasound to quantify the lumbar spinal canal. *British Journal of Radiology*, *54*, 870–874.

NACHEMSON, A. and ASZTÉLY, M., 1981. Use of diagnostic ultrasound to measure the lumbar spinal canal. *British Journal of Radiology*, *54*, 1010.

1981, *British Journal of Radiology*, *54*, 1117–1121 DECEMBER 1981

Proceedings of The British Institute of Radiology*

Radiobiology work-in-progress: hyperthermia

Abstracts of papers presented at the meeting held on Friday, May 22, 1981

at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG

Chairman: Professor R. J. Berry

The effects of hyperthermia on the non-proliferating cells of mouse intestinal mucosa, by S. P. Hume, J. C. L. Marigold and A. S. Michalowski.
Role of low pH, lactic and beta-hydroxybutyric acids in cell killing by hyperthermia, by J. Lunec, R. Parker and S. R. Cresswell.
The influence of hyperthermia on tumour blood flow and hypoxic cell fraction, by F. A. Stewart and A. C. Begg.
Effects of the combination of hyperthermia with cytotoxic agents on normal mouse bone marrow, by D. J. Honess and N. M. Bleehen.
Induction of thermal resistance by fractionated hyperthermia, by M. P. Law, S. B. Field, R. G. Ahier and S. Somaia.
Does local hyperthermia increase the incidence of distant metastases? Data for five mouse tumours, by Sally A. Hill and Juliana Denekamp.
The assessment of unwanted radiation around RF inductive applicators, by P. Carnochan and C. H. Jones.
Radiofrequency diathermy for heating mouse tumours, by M. C. Joiner, B. Vojnovic and R. Davies.
Equipment for the clinical application of hyperthermia, by P. B. Dunscombe, B. M. Southcott, K. Gammampila and A. J. Stacey.
Hyperthermia in the clinic, by B. M. Southcott, P. B. Dunscombe, K. Gammampila and A. J. Stacey.
Microwave-induced intracavitary hyperthermia for carcinoma of the cervix, by J. W. Hand, P. R. Blake, H. E. Lambert and S. B. Field.

THE EFFECTS OF HYPERTHERMIA ON THE NON-PROLIFERATING CELLS OF MOUSE INTESTINAL MUCOSA

By S. P. Hume, J. C. L. Marigold and A. Michalowski

MRC Cyclotron Unit, Hammersmith Hospital,
DuCane Road, London W12 0HS

The effects of local hyperthermia on different components of mouse intestinal mucosa have been investigated. The intestine was heated by immersion in Krebs-Ringer solution at various times after intraperitoneal injection of ^{3}H-thymidine and thermal injury was assessed by measuring loss of label. The results have been compared with histological observations and also with earlier data on crypt loss.

Heating at 42°C for up to one hour had no observable effect. When the intestine was heated at 43°C, 14 hours after labelling, the loss of label was very similar to the loss of crypts with regard to both the degree and the time over which the response occurred. The threshold heating time to cause an effect was between 20 and 30 min and the response was complete by 6–8 h after treatment.

If, however, intestine was heated at 43°C either 65 or 72 h after injection of ^{3}H-thymidine, the threshold heating time to cause an effect was between ten and 20 min. The loss of label was not accompanied by crypt damage (for example, 50% of radioactivity could be lost without any corresponding loss of crypts).

Both histological examination and the labelling experiments indicate that the non-proliferative cells of intestinal mucosa lining the lumen are much more susceptible to thermal injury than the crypt cells. Thus, although crypt loss may be used in the assessment of thermal damage to small intestine, the data would be an underestimate of early mucosal injury and the functional integrity of the intestine.

ROLE OF LOW PH, LACTIC AND BETA-HYDROXYBUTYRIC ACIDS IN CELL KILLING BY HYPERTHERMIA

By J. Lunec, R. Parker and S. R. Cresswell

MCR Cyclotron Unit, Hammersmith Hospital,
DuCane Road, London W12 0HS

Studies were made of the effects of variation in pH, and of the acid metabolites lactic acid and β-hydroxybutyric acid, on the response of various cell lines to heat treatment.

For a given set of handling conditions and method of pH adjustment, the influence of pH on cell killing by hyperthermia varied considerably between cell lines. In general the increased sensitivity to heat at low extracellular pH was much greater at 42°C than 44°C. A major contribution to the increased pH effect at 42°C was the inhibition or delay of the development of thermal tolerance during heat treatment.

Intracellular pH was estimated by measuring the partitioning of the labelled weak organic acid 5,5-dimethyl-2,4-oxazolidinedione (DMO) between the inside and the outside of the cells. When the pH of the medium was lowered from 7.4 to 6.7 a reduction in intracellular pH was found for all the cell lines studied. There was no correlation between the extent of reduction in intracellular pH and the effect of extracellular pH on the sensitivity of the cells to heat treatment.

The effect of pH on cell killing by hyperthermia at 42°C or 44°C was the same whether the pH of the medium was lowered by reducing the amount of sodium hydroxide or by adding the physiologically relevant metabolites, L-lactic acid and β-hydroxybutyric acids. All methods of reducing the pH of the medium reduced the intracellular pH to the same extent.

---

*No reprints of these Proceedings are available.

THE INFLUENCE OF HYPERTHERMIA ON TUMOUR BLOOD FLOW AND HYPOXIC-CELL FRACTION

By F. A. Stewart and A. C. Begg

Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

The thermal enhancement ratio (TER) for combined heat and X rays in a murine sarcoma (Sa FA) was 1.5–1.7 for single doses with 42.5°C applied for 1 h immediately after X rays. This TER was reduced in fractionated treatments to 1.0 for two daily fractions and 1.1–1.3 for five fractions. Changes in tumour blood flow and hypoxic-cell fraction have been investigated as possible reasons for the observed reduction in TER with fractionation.

Relative tumour perfusion was measured using the ^{86}Rb extraction technique. Relative perfusion was significantly decreased over the period 1–3 days after heating (42.5°C for 1 h), returning to normal by seven days.

Hypoxic-cell fractions were estimated for heated and unheated tumours by comparing dose-response curves for growth delay using oxic and clamped (hypoxic) tumours. There was an indication of an increased hypoxic fraction 24 h after heating.

These data suggest that a decreased tumour blood flow and increased hypoxic fraction occurred 24 h after a single heat treatment of 42.5°C for 1 h. Therefore both factors probably contributed to the observed decrease in radiation sensitivity of the tumour after heating, resulting in the small TER seen for fractionated treatments of X rays plus heat.

EFFECTS OF THE COMBINATION OF HYPERTHERMIA WITH CYTOTOXIC AGENTS ON NORMAL MOUSE BONE MARROW

By D. J. Honess and N. M. Bleehen

MCR Unit and University Department of Clinical Oncology and Radiotherapeutics, Hills Road, Cambridge CB2 2QQ

A limiting toxicity of several cytotoxic agents, whose tumouricidal effects are enhanced by hyperthermia, is to the bone marrow. The effects of combining heat with cyclophosphamide (Cyclo) or BCNU on normal, undifferentiated mouse bone-marrow stem cells were studied using the spleen colony-forming assay developed by Till and McCulloch (1961). Survival was assayed at two hours and 24 h after treatment. Unanaesthetized, unrestrained C3H/He mice were given whole-body hyperthermia for 45 min at a rectal temperature of 41±0.2°C by enclosing them in an incubator. Stem-cell survival was unaffected by heat alone. Drug doses were chosen to give a reduction in survival of up to one decade at room temperature, and drugs were given IP at the start of heating.

For Cyclo, the dose-response curve for unheated mice with doses up to 200 mg/kg was exponential after an initial shoulder when assayed at two hours and was exponential at 24 h. Heat increased the damage at doses above 100 mg/kg when assayed at two hours and at all doses when assayed at 24 h; however, for 200 mg/kg, the increase was of the same order at both assay times. The dose-reponse curves for BCNU (unheated mice) with doses up to 60 mg/kg were exponential whether assayed at 2 hours or 24 h, and heat potentiated damage at all doses, but potentiation was much greater when assayed at 24 h than at two hours.

These data indicate the need for directly comparable tumour data to allow therapeutic ratios to be estimated for the combined treatments.

REFERENCE

Till, J. E. and McCulloch, E. A., 1961. A direct measurement of the radiation sensitivity of normal mouse bone marrow cells. *Radiation Research*, *14*, 213–222.

INDUCTION OF THERMAL RESISTANCE BY FRACTIONATED HYPERTHERMIA

By M. P. Law, S. B. Field, R. G. Ahier and S. Somaia

MRC Cyclotron Unit, Hammersmith Hospital, Du Cane Road, London W12 0HS

Hyperthermia either alone or in combination with radio- or chemotherapy is already being used in fractionated regimens to treat human tumours. Although it is known that a single heat treatment induces resistance to subsequent hyperthermia in cells and tissues, there is little information about the effects of more than two heat treatments.

The response of the mouse ear to multiple heat treatments at 43.5°C was investigated. Hyperthermia was achieved by immersing the ears in heated water. The effect of 1–10 priming treatments was measured by determining the duration of a subsequent test treatment required to cause necrosis in 50% of the ears heated.

A single priming heat treatment, which itself caused no detectable effect, induced transient resistance to the test treatment. The maximum effect was observed 22 h after a 20 min priming treatment, when the test treatment had to be increased by a factor of 2.4 compared with a single heat treatment (Law *et al.*, 1979).

To test if resistance could be increased by subsequent hyperthermia, a second priming treatment was given at the time of maximum resistance, *i.e.* one day after a 20 min treatment. A second treatment of 70 min, which caused no visible effect in resistant ears but which would cause necrosis if given as a single treatment, was used. Resistance after the two priming treatments was similar in both magnitude and time course to that observed after a single 20 min priming treatment.

Resistance induced by several 20 min priming treatments, given at daily intervals, was measured by giving a test dose at 24 h after the last priming treatment. Two, five or ten treatments induced the same degree of resistance as that induced by one 20 min treatment.

These results indicate that the maximal thermal resistance induced by a single heat treatment is not further increased by giving repeated daily treatments.

REFERENCE

Law, M. P., Coultas, P. G. and Field, S. B., 1979. Induced thermal resistance in the mouse ear. *British Journal of Radiology*, *52*, 308–314.

DOES LOCAL HYPERTHERMIA INCREASE THE INCIDENCE OF DISTANT METASTASES? DATA FOR FIVE MOUSE TUMOURS

By Sally A. Hill and Juliana Denekamp

Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN

Local hyperthermia may increase the probability of local tumour control, but it has been suggested that it might also enhance the spread of disease. At present, the data available in the literature are conflicting.

We have performed two types of study; a retrospective analysis of data obtained incidentally from regrowth delay experiments, and prospective studies designed specifically to investigate the effect of heat on the incidence of lung metastases. In the first case tumours were treated with a range of palliative doses of X rays either alone or in combination with heat (42.8°C for one hour). Since tumours regrew at different times according to the effectiveness of the treatment, some animals may have been killed before metastases had time to grow to a macroscopically visible size. Only one tumour, out of five, showed a significantly increased incidence of metastases, *i.e.* one out of the 17 treatment schedules used; this was the CA SQ D, when heated immediately before irradiation.

The prospective studies were designed to give local control of the primary tumours. Neither heat applied immediately before or after irradiation of the CA SQ D resulted in a significant change in incidence of metastasis. However, whole-body heating did produce a marginally significant increase. Fractionated hyperthermia (four heat doses + curative radiation) also resulted in no significant change in the metastasis frequency of the SA F.

These data would suggest that local heating combined with radiation does not result in an increased risk of metastatic spread.

THE ASSESSMENT OF UNWANTED RADIATION AROUND RF INDUCTIVE APPLICATORS

By P. Carnochan and C. H. Jones

Physics Department, Royal Marsden Hospital,
Fulham Road, London SW3

During the development of clinical hyperthermia systems which utilize electromagnetic fields and waves, attention must be paid to the possible exposure of operating personnel and nursing staff to potentially harmful levels of electromagnetic radiation. It is also important, where localized hyperthermia is intended, to assess the effects of electromagnetic fields induced in regions surrounding the treatment volume, and where indicated to evaluate screening methods by which such effects may be minimized.

Currently accepted and proposed American and West European guidelines for safe exposure are based upon the thermogenic effects of acute whole-body plane-wave irradiation. Serious problems of interpretation arise when near-field exposure is considered, as is necessary for RF inductive heating. Furthermore, measurements of the exposure field cannot always be expected to correlate with fields induced within body tissues. However, where the predominant bio-effects are connected with RF magnetic fields, useful information can be obtained from a survey of the exposure field.

Using a Narda model 8602 broadband radiation monitor incorporating an isotropic probe sensitive to magnetic fields, a survey has been made of the area surrounding a prototype 27 MHz inductive heating system based on modified short-wave diathermy apparatus. Sources of RF current making significant contributions to the exposure field have been identified.

From the data obtained it can be concluded that the exposure regions of greatest significance from a safety point of view are highly non-uniform and indicate that exposure to levels in excess of current safety guidelines is likely to be correspondingly localized.

Considering the large size of the Narda magnetic-field probe compared with field divergence, accurate quantification of the fields in regions corresponding to those close to intended treatment volumes was not possible. Measurements taken indicate the usefulness of a closer study of these regions using a smaller anisotropic probe, which would be used to evaluate screening materials employed to reduce the magnitude of fields likely to be induced in tissues not adapted to large amounts of thermal stress.

RADIOFREQUENCY DIATHERMY FOR HEATING MOUSE TUMOURS

By M. C. Joiner, B. Vojnovic and R. Davies

Gray Laboratory, Mount Vernon Hospital, Northwood,
Middlesex HA6 2RN

Temperature differences of up to 2°C have been reported within tumours heated by immersion in hot water. Radiofrequency (RF) diathermy is being developed to obtain more uniform heating. We have found that RF electric fields (27.12 MHz) together with immersion in warmed electrolyte gives the most uniform temperature distributions across tumours implanted intramuscularly in mouse limbs.

RF voltage was applied to a pair of parallel, circular (2 cm diameter) copper plates. The tumour-bearing leg was heated between the plates which were electrically coupled to the tissue by ECG jelly, or by weak saline (0.043% w/v) which was found to be approximately electrically equivalent to tumours at 27 MHz.

With the RF field turned off, temperatures were measured simultaneously at six points in each tumour. A single fine probe (0.5 mm diameter) has been constructed to do this, consisting of six thermocouple junctions at 1.5 mm intervals.

Tumours were initially heated by RF only, using ECG jelly for electrode-tissue coupling, and the temperature at the tumour core could be raised by 44°C within five minutes using an applied field of 1 W cm^{-2}. However, temperatures in the tumour periphery remained 15–20°C lower; the temperature measured at the skin was close to ambient (18°C).

When RF heating was combined with immersion in weak saline bolus, the temperature differential was reduced to less than 1°C. This was further improved to ±0.15°C by circulating pre-heated saline around the immersed leg.

The effect of blood flow was assessed by killing animals *in situ* during heating. The cessation of blood flow led to an increase in tumour-core temperature by appoximately 2°C when heating by RF or hot-water immersion.

Temperatures in individual tumours varied with time by up to 3°C during one hour heat treatments if the RF was applied at a constant power. A thermostatic control unit to modify the power to each tumour in a multi-irradiation set-up is under development to overcome this problem.

EQUIPMENT FOR THE CLINICAL APPLICATION OF HYPERTHERMIA

By P. B. Dunscombe, B. M. Southcott,
K. Gammampila and A. J. Stacey

Charing Cross Hospital, London W6 8RF

A commercially available microwave generator has been modified to provide equipment suitable for the hyperthermic treatment of malignant disease. The applicator is a TE_{10} waveguide employing water as a dielectric. Such a technique allows the 434 MHz beam to be restricted to a cross section of 8 × 4 cm. The large degree of skin heating which is a consequence of localized microwave irradiation is offset to some extent by forced-air convective cooling. This approach has been shown both theoretically and experimentally to be effective. Temperatures can be measured at two sites.

Skin temperature is measured with a thermocouple stretched across the end of the guide. Tumour temperature is monitored with a thermocouple housed in a 0.5 mm diameter steel needle. Although a small artefact is apparent when these thermometers are used in the presence of the microwave beam, this is not due to localized heating of the probes and has not been found to be a major disadvantage of the equipment. The equipment has been assessed with the aid of a tissue-equivalent phantom and an indication of the temperature profiles likely to be produced *in vivo* has been obtained.

HYPERTHERMIA IN THE CLINIC

By B. M. Southcott, P. B. Dunscombe,
K. Gammampila and A. J. Stacey

Charing Cross Hospital, London W6 8RF

A review of current experimental data relating to the possible therapeutic effects of hyperthermia in the treatment of cancer emphasizes the difficulties in extrapolating from the experimental to the clinical situation and the need for early clinical studies. Equipment producing local microwave hyperthermia (434 MHz) has been used in a pilot study with eight patients.

Four of these had carcinoma of the breast and four, soft-tissue sarcomas. Three of the sarcoma group had radiotherapy concurrently. In each case heat was applied for 30 min once weekly. A total of 45 separate treatments was given during which tumour and skin temperatures were monitored continuously with thermocouple probes. The equipment performed reliably, was easy to use and the treatment was acceptable to the patients. The average temperatures of the tumour and skin were 45.0° and 42.0°C respectively.

The results of treatment were difficult to interpret in this small heterogeneous group lacking controls but, of the five patients receiving heat alone, one had a complete response, two had partial responses and two had no response. This rather poor response rate was probably due to under-treatment.

A previous study with pigs suggested that with relatively short treatment times a temperature of at least 47.5°C is needed to produce significant cell kill.

MICROWAVE-INDUCED INTRACAVITARY HYPERTHERMIA FOR CARCINOMA OF THE CERVIX

By *J. W. Hand, *†P. R. Blake, †H. E. Lambert,
*S. B. Field and ‡J. W. Hopewell

**MRC Cyclotron Unit and* †*Department of Radiotherapy,*
Hammersmith Hospital, Du Cane Road, London W12 0HS
and
‡*Research Institute, Churchill Hospital, Headington,*
Oxford OX3 7LJ

Carcinoma of the cervix is increasing in incidence. Since more early-stage disease is seen now than in the past, the failure of local control is becoming a more frequent problem despite improvements in the accuracy of staging and radiotherapy planning.

It is thought that squamous cervical tumours contain a high proportion of hypoxic cells; hyperthermia may, therefore, prove to be a useful treatment. There are reports in the literature of the use of electromagnetic waves to raise the temperature in this site (*e.g.* 434 MHz external applicators and radiofrequency heating by interstitial electrodes). In several early clinical studies favourable responses have been observed in tumours treated by hyperthermia in combination with radiotherapy.

We have designed microwave applicators that can be inserted into the standard plastic afterloading tube used with linear caesium sources for conventional intracavitary treatment. These applicators operate at frequencies of 800–1000 MHz and use a dielectric encapsulated dipole as the radiating element. Temperatures are measured by fine-wire thermocouples incorporated into the afterloading tube. In clinical use the device will be inserted into the afterloading tube, without further trauma to the patient, approximately four hours after intracavitary radiotherapy.

A description of these applicators was given and the results of preclinical tests in phantom materials and pigs were presented.

Radiology of the colon

Abstracts of papers presented at a meeting held on Thursday, May 14, 1981 at The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

Chairman: Dr. H. B. Meire

Colonic radiology—what the surgeon needs to know, by C. Wastell (*no abstract received*).
When enema, when endoscopy, by C. B. Williams.
What type of enema and when, by C. I. Bartram.

WHEN ENEMA, WHEN ENDOSCOPY

By C. B. Williams

St. Mark's Hospital, City Road, London EC1

Barium enemas are easy to perform but often difficult to interpret. Colonoscopy is easy to interpret because of colour and the employment of biopsy techniques; however, even in expert hands, 25% of colonoscopies are technically very difficult and most patients require some sedation. Fibre-sigmoidoscopy without sedation can reach the splenic flexure in 50% of cases, thus covering the problem area for the radiologist, the sigmoid colon—so often tortuous or affected by diverticular disease. Studies in 300 patients having colonoscopy with CO_2 for rapid gas absorption, followed by immediate barium enema, show that by combining fibre-sigmoidoscopy immediately before barium enema the diagnostic accuracy of X ray is equal to that of colonoscopy, which tends to miss lesions in the capacious right colon.

Certain patients are well suited to colonoscopy as the primary procedure, especially those where any abnormality is likely to be minor and therefore radiologically invisible, or where biopsies are essential; additionally, patients with a high probability of polyps can gain the advantage of immediate polypectomy. Thus, we suggest primary colonoscopy for small children with possible inflammatory bowel disease, screening examinations for polyposis or follow-up of chronic colitis at high cancer-risk, patients with continued rectal bleeding or persistent iron deficiency anaemia of gastrointestinal origin.

There should be a working relationship between practitioners of colonoscopy and enthusiasts for the barium enema, such that each patient gets the examination for which he is best suited, either from experience of previous examinations or by clinical indication.

Proceedings of The British Institute of Radiology

WHAT TYPE OF ENEMA AND WHEN

By C. I. Bartram

St. Mark's Hospital, City Road, London EC1

The double contrast barium enema (DCBE) is now established as the ideal method for the radiological study of the colon and rectum. Bowel preparation, barium suspension, the amount given, rectal drainage, method of air insufflation, film sequence and positioning are critical factors in achieving an examination of technical excellence, which will provide the maximum information possible. The image may be degraded by overlapping loops, residue or barium artefacts, but most frequently by excess barium pooling in dependent parts. The accuracy of any film can be judged from how much of the bowel is seen in double contrast. Where there is pooling of barium the accuracy is downgraded to that of single contrast. Comparisons with colonoscopy show that significant lesions, adenomas more than 7 mm in size, are liable to be missed in the following situations: (1) in the sigmoid colon, especially when affected by diverticular disease; (2) in redundant loops; (3) close to the ileo-caecal valve; and (4) in the hepatic flexure.

The examination of the colon when the rectum has been removed is much more difficult as there are problems in forming an effective seal with a colostomy, and retrograde filling of the bowel induces marked peristalsis. Cleansing water enemas are particularly difficult in these patients. IV relaxants are essential to allow filling with barium and air and to obtain sufficient distension of the bowel. The quality of the examination seldom matches that of a normal DCBE.

When colitis is known to be present the information required from a barium enema is mainly the extent and severity of the colitis. Bowel preparation might be harmful in the presence of a colitis and would certainly be uncomfortable. To demonstrate minor changes the bowel must be examined in double contrast. The instant enema does not require bowel preparation and is a double contrast enema that works well when ulcerative colitis is diffuse and continuous, but not so well in Crohn's disease when the colitis is discontinuous. It is contra-indicated in toxic megacolon and perforation. Plain films are invaluable in assessing an acute attack of colitis. The presence of gas in the bowel will show if the mucosa is ulcerated or not. Gas may be absent, in which case it can be added by air insufflation. The "air enema" may be used in an acute attack of colitis when the absence of gas on the plain film means that the mucosal state cannot be assessed.

Water-soluble contrast media have two advantages—low viscosity and relative safety if they enter the peritoneal cavity. Contrast medium may be diluted with three parts of water. It will still be of sufficient radiographic density but is cheaper and less hypertonic, which is the main hazard (1 : 5 dilution of gastrografin is isotonic). A water-soluble contrast enema is used where there is a suspected perforation, fistula, or in megacolon and Hirschsprung's disease to outline the unprepared bowel.

There are a number of ways to examine the large bowel. When requested to do so, the radiologist must consider the patient's clinical condition and what sort of information is required before selecting the appropriate type of enema.

Book review

A History of X Rays and Radium. By R. F. Mould, pp. 100, 1980 (Building & Contract Journals Ltd., Sutton, Surrey), £12·95.
ISBN 0-617-00355-6

This is a "fun" book. The reviewer usually has to derive his pleasure from his interest in the subject of a book, and occasionally from an exciting idea or an elegant presentation. In this case Dr. Mould has provided a rare and unexpected entertainment. The book provides the same kind of excitement in discovery as the better sort of comics did, when we had not long learnt to read. Like the comic, the pages do not seriously have to be taken in sequence. Open the book at almost any point and a jumble of fascinating historical pictures and interesting snippets of information, each a complete story in itself, are laid out attractively in the mellow tones of the old sepia prints.

The author has in fact collected together in one volume an unusual miscellany relating to the discovery and early use of X rays and radium, covering a period of some 40 years. The first chapters deal in a fairly anecdotal manner with the major historical events and investigations. The scholar will be a little disappointed if he takes the title at its face value and expects a systematic and critical review. Others will be less concerned. There is a unique chapter describing the development of the units, such as the Rutherford, the uranie and the mache, in which activity, X and γ rays could be or were in fact quantified. This provides a rare insight into the preoccupations and habits of thought of the early practitioners. There are some 30 pages of pictorial history with informative and entertaining annotations. A postscript briefly brings us up to date in the subject, but is rather preoccupied with therapeutic developments, and the radiologists will have to forgive the omission of a mention of computed tomography, even though it can hardly be neglected as a major contribution to the application of X rays in medicine. Apart from a comprehensive and illustrated index, the book closes with some 15 pages of advertisements culled from the publications of the period. These provide another unusual opportunity to obtain a glimpse of those aspects which were considered to be of value and importance in the early years.

The book is intended for "experts" in the field of radiation applied to medicine, as well as those with an interest in history. Certainly, few non-specialists will know what is meant by such details as the points A and B in the Manchester dosage system, but there is so much else that they can readily appreciate that the book is likely to be enjoyed by a far wider audience than the author intended. Well-thumbed copies may be expected to find their way into the more sophisticated medical waiting rooms, and into school science departments where they might well help to bring alive that small part of the "A" level syllabus. For experts such as doctors, physicists, radiographers and scientific historians, the bibliography and illustrations will provide a notable source of reference. The BJR reader in particular is recommended not to miss the opportunity of obtaining a copy while they are available.

M. F. COTTRALL.

Obituary

Ralston Paterson

Emeritus Professor J. Ralston K. Paterson, C.B.E., M.C., M.D., F.R.C.S.(Ed), Hon. F.R.C.R. (or R.P. as he was known to his colleagues and as he would wish to be known) died on August 31, 1981, at his farm near Moffat, at the age of 84. Born in Edinburgh, a "son of the manse", he gained the M.C. in the first world war before graduating, with honours, at the Edinburgh Medical School. He gained medical and radiological experience in South Africa, the Mayo Clinic and the Edinburgh Royal Infirmary (where he was acting director of the Radiology Department) before becoming, in 1931, Director of the Holt Radium Institute, a post which he held, under various titles and with great distinction until his retirement in 1962 when he became an equally successful farmer.

Within five years he had raised a locally respected institute to be in the view of many, the world's leading radiotherapy centre. At the same time he was an acknowledged leader of a small group of British radiologists changing radiotherapy from a mainly palliative procedure into a major curative agent in the treatment of cancer.

To many, R.P.'s name will be immediately associated with the widely adopted Radium Dosage System of which he was joint author with his physicist colleague, H. M. Parker. In fact, this was but one of the many important contributions to radiotherapy which he made or inspired others to make. Alive to the vital importance of accurate radiation dosimetry he nurtured the infant medical physics and greatly encouraged and aided its development. Believing that, in their response to ionizing radiations, patients were more alike than different, he argued that success for radiotherapy required the establishment of optimum dosage levels from observation of the results of large numbers of cases comparably treated to known dosage levels. To this end he pioneered the centralized radiotherapy department with peripheral diagnostic and "follow up" clinics. In addition to the radium system he developed (with J. L. Dobbie) what was then called "small field, beam-directed" X-ray therapy and he enlarged the roles of the medical records and medical statistics departments. Always he tried to make his methods quantitative and well defined so that they could be carried out anywhere and were not (as had often been the case) dependent upon the unique (and often non-transferable) experience of a particular individual. In this way his effect on the advance of radiotherapy was enormous.

Realizing the importance of research, he not only encouraged it among his clinical colleagues, but, early in his directorship, set up two fundamental research groups which, under Edith Paterson and Walter Dale, not only made important contributions to radiobiology, but were the sure foundation upon which the Paterson Research Laboratories were built. Later he pioneered clinical randomized trials for the better evaluation of alternative techniques and, realizing the importance of public education about cancer, developed (with John Wakefield) a wide ranging regional education scheme with an associated small research group to assess its efficacy and advance its techniques. Outside his institute he played a leading part in the separation (to the ultimate benefit of both parts) of radiology into its two major components of diagnostic radiology and radiotherapy and in ensuring their continued close association as equal members of the Faculty of Radiologists of which he was an architect, founder member and first radiotherapist president.

International fame and honours soon came his way. In 1943 he was invited by the Australian government to advise it on radiotherapy organization; in 1949 he was awarded the C.B.E. and the next year he was the first (and is still the only) radiotherapist to be President of the International Congress of Radiology. First professor of radiotherapy in the University of Manchester, memorial lecturer, gold medallist; honorary memberships—he received them all with satisfaction, pleasure and with a simple acceptance that he deserved them! He knew his worth, accepted its responsibility and had not the slightest conceit. He was a great man and he was a big man: big of physical frame, of intellect, of energy and of heart and magnaminity.

R.P.'s interests were relatively limited because his work at the time was his consuming passion—radiotherapy in Manchester, farming when he moved to Dumfriesshire. This passion for his work coupled with his energy and his preparing every case in the greatest detail ("doing his homework" he called it) made him a formidable and often irresistable opponent in argument or negotiation. In his early days especially he was like some powerful rugby forward who, getting the ball on "the 22", heads unstoppably for the line brushing off tackles as he goes. The success he thus secured did not endear him to the local medical "establishment" determined to keep radiotherapy and radiotherapists in their "proper" (*i.e.* subsidiary) place. But he scored his points and radiotherapy and mankind were the winners.

He was a great organizer and an inspiring leader with a flair for picking the best people from among the large numbers who sought posts on his staff or training under him. A recent count (from memory) showed that over 60 of his trainees hold, or have held, directorships of important radiotherapy departments in this or in 16 other countries across the world. A further factor in his success was his ability to see the essentials amid the welter of information and to crystallize diffuse discussion into a working policy. Generally his judgements were sound but he was never afraid to admit an error and, with a curt "cut your losses", would set about the establishment of a better policy.

Detractors of the "Manchester" methods alleged that they constituted an impersonal "sausage machine". Nothing could be further from the truth. For all his dedication to the scientific approach, R.P.'s first thoughts were always for the patient as an individual to be treated with the utmost courtesy and consideration and one whose anxieties and need for reassurance were fully understood. He insisted that clinics should run to schedule and that where waiting was unavoidable the reason should be explained. Long before such amenities were a feature of Out Patients' Departments, R.P. invited a group of local ladies to serve cups of tea to waiting patients suggesting that they should wear pretty frocks, rather than uniform overalls, "to bring a little brightness and comfort" to anxious, often frightened people. Nearly 50 years later that service continues, a small memorial to a caring man.

As we have said, R.P. was a master at choosing the best people and he never chose more wisely nor more fortunately than when he married Edith Irvine Jones who had graduated with him in 1923. For E.P. (as she is affectionately known) was not only a wonderful wife and mother but was his scientific guide, encourager and prop and, in the last months, his devoted nurse and comforter. To her, to their daughter and two sons and to their grandchildren who were such a joy to him goes our deepest sympathy in the loss of a dear and fine husband and father. Those of us who have been privileged to work with him and to know him have lost an inspiring leader and a good friend. Mankind has lost one who served it better than most will every know. We are richer for his having lived and poorer for his passing.

W. J. MEREDITH.

Book review

Dictionary of Medical Ethics. Ed. by A. S. Duncan, G. R. Dunstan and R. B. Welbourn, pp. 459, 2nd edit., 1981 (Darton, Longman and Todd, London), £12·50.
ISBN 0-232-51492-5

The first edition of the *Dictionary of Medical Ethics* was published in 1977 and it rapidly became the authoritative text on the subject. Within four years its initial and sustained success demanded a second edition. There has been revision of the text and new entries which have made the volume more definitive. Two essays at the beginning of the volume have been an important addition to this new edition. The first is on the scientific basis of medical practice. It is emphasized that as medical science provides most of the framework of modern medicine, doctors must be thoroughly grounded in it if, as they are morally obliged to do, they are to serve their patients to the best of their ability. People are entitled to know the possibilities and limitations of medical practice and any discussion of medical ethics must start with a full knowledge of the scientific aspects of the matter under discussion.

The second essay is on medical ethics, by which is meant the obligations of a moral nature which govern the practice of medicine and the relationship between practitioner and patient or volunteer. The purpose of medical ethics is to create and maintain trust between practitioner and patient, between practitioner and practitioner and the trust of society as a whole in the profession corporately. It is important that the profession develops its ethics to accommodate new demands and circumstances, passes on its ethics to the next generation of practitioners, helps and sustains its members in the practice of medicine and disciplines them when by non-ethical conduct they deny their patients the standard of service they may properly expect. Historically the spread of Western medicine carried with it ethical values as well as science and skills and these essentially human values were readily absorbed into the medical ethics of other cultures. It was then possible to draw up declarations on various aspects of medical practice which could be accepted the world over. They are all loosely derived from the "Hippocratic oath". Various bodies such as the Royal Colleges have also issued Codes of Practice for the guidance of their members. These Declarations and Codes are given in the text of this dictionary.

There are 148 contributors to this dictionary, the large majority of which are doctors, one being a diagnostic radiologist. There are also clergy, nurses, lawyers, journalists, pharmacologists, etc., but no radiotherapist. Each entry in the text is clear and precise with the name of the contributor appended. Most entries have a useful bibliography. The first entry is Abortion and the last the World Health Organization. The comprehensive list of subjects in between include such topics as African Medicine, Amniocentesis, Human Experimentation, Artificial Insemination, Clinical Trials, Confidentiality, Consent, Death, Human Rights, Research Ethical Committees, Screening, Telling the Truth, etc. There is relatively little relating to ionizing radiation and there is no discussion of the implications to medical practice and research of the recent introduction of a licensing system by the Administration of Radioactive Substances Advisory Committee. As the text is presented in dictionary form, it is sometimes difficult to find the required information. For instance there is no direct entry for "Volunteers" used in research projects; the entry comes under "Human Experiment—Dependent Subjects."

This dictionary is a valuable contribution to the field of medical ethics. It should find a place in the library of radiodiagnostic and radiotherapy departments where it would be hoped it would be consulted frequently.

F. G. M. ROSS.

Forthcoming events and notices

Meeting announcements by organizations other than The British Institute of Radiology and its associated bodies are accepted for a charge of £1·50 per line per edition. Copy deadline for inclusion in this section is the 20th of the penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. F. Secretan, Managing Editor, The British Journal of Radiology, 36 Portland Place, London W1N 3DG.

Burrows and Leeds "Neuroradiology"

The publishers have had to withdraw this book from circulation because of production defects. Copies are being recalled from bookshops. If you have bought a copy of *Neuroradiology*, please return it to the bookseller. The book is being reprinted and will be available in the near future.

Churchill Livingstone, Robert Stevenson House, 1–3 Baxter's Place, Leith Walk, Edinburgh EH1 3AF, UK.

Fellowships and Grants for Cancer Research

The International Union against Cancer invites applications for Yamagiwa-Yoshida Memorial International Cancer Study grants (deadline December 31) and International Cancer Research Technology Transfer Programme Grants. Details and application forms from: UICC, rue du Conseil-General 3, 1205 Geneva, Switzerland.

The International Agency for Research on Cancer (World Health Organization) invites applications for training fellowships in 1982/3 from junior scientists wishing to be trained in the fields of epidemiology, biostatistics and environmental carcinogenesis (both chemical and viral). Details and application forms from: The Head of the Research Training and Liaison Programme, 150 cours Albert-Thomas, 69372 Lyon Cedex 02, France. Deadline January 31 1982.

British Medical Ultrasound Society

The 1981 Annual Meeting will be held on December 14–15 at the University of London Union, Malet Street, London WC1.

Quantities and Units for use in Radiation Protection

Scientific meeting and exhibition, National Physical Laboratory, Teddington, Middlesex, Tuesday, January 26, 1982. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

Radiopharmaceuticals and Radiopharmacology

Under the auspices of the European Joint Committee on Radiopharmaceuticals of the European Nuclear Medical Society and the Society of Nuclear Medicine Europe a course on radiopharmaceuticals and radiopharmacology will be held in Berlin, DDR from January 27 to 31, 1982.

This course is designed for medical graduates and graduates in the biological sciences who are concerned with *in vivo* nuclear medical procedures. The course would also be suitable for pharmacists, chemists and other paramedical personnel who are training for work in this field.

Further details can be obtained from the course organizer: Dr. Harald Deckart, Chefarzt der Nuklearmedizinische Klinik und Poliklinik, Wiltbergstrasse 50, 1115 Berlin-Buch.

The Mayneord Symposium

Friday February 19, 1982 at 10.30. This meeting is being organized by the BIR Council in honour of the 80th birthday of Professor W. V. Mayneord, C.B.E., F.R.S. at the Royal Society, 6 Carlton House Terrace, London SW1. The theme for the meeting will be "The future in radiology" reviewed by a number of distinguished speakers including: Dr. T. A. Connors (MRC Toxicology Unit), Sir Frederick Dainton, F.R.S., Professor J. F. Fowler, Dr. R. H. Clarke (NRPB), Professor G. H. du Boulay, Professor R. J. Berry, Professor G. L. Brownell (Massachusetts General Hospital), Dr. P. N. T. Wells, Professor I. Isherwood, Dr. M. J. Day, Professor B. S. Worthington, Mr. G. Thomson (National Gallery).

BIR Radiobiology Meetings

Future meetings in the Institute will comprise a general meeting on February 26, 1982 and "Late damage to normal tissues after radiotherapeutic doses" on May 21, 1982. Titles of proffered papers for the February meeting should be sent to Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, by December 9, 1981, and for the May meeting preferably by January 22, 1982.

The Clinical Value of Mammography

Cambridge, February 26, 1982. This meeting will be of interest to radiologists, surgeons and other clinicians dealing with breast disease. For further information please write to: Dr. A. H. Freeman, Department of Radiology, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ.

The Natural Radiation Environment

Tuesday, March 30, 1982, at the Central Electricity Generating Board, Sudbury House, 15 Newgate Street, London EC1. Organized by the Society for Radiological Protection. Enquiries: Prof. J. H. Martin, Dept. of Medical Biophysics, Blackness Laboratory, University of Dundee, Dundee DD1 4HN.

British Nuclear Medicine Society
Annual Scientific Meeting

April 19–21, 1982, at Imperial College, London SW7. Closing date for abstracts: February 1, 1982. Forms can be obtained from the Conference Secretary, 22 Leinster Avenue, East Sheen, London SW14 7JP.

European Society of Pediatric Radiology
19th Congress, Prague, April 22–24, 1982

Organized by the European Society of Pediatric Radiology, Czechoslovak Medical Society J. E. Purkyně, Czechoslovak Radiologic Society and the Czechoslovak Pediatric Society. Deadline for applications and abstracts: December 30, 1981. Information: Czechoslovak Medical Society J. E. Purkyně, 19th Congress of the European Society of Pediatric Radiology, Vítězného února 31, 120 26 Praha 2, Czechoslovakia.

Society for Radiological Protection
Third International Symposium—Inverness 1981

June 6–11, 1982. Main topics: radiation and risks; radiobiology and epidemiology; instrumentation and equipment; design of facilities; radioactivity in the environment; education and public information; legal and regulatory aspects; accident management; non-ionizing radiation; medical techniques. Brochure from Symposium Organizer, SRP International Symposium, c/o NRPB Harwell, Didcot, Oxon OX11 0RQ.

Forthcoming events and notices

3rd World Federation Meeting for Ultrasound in Medicine and Biology: July 26–30, 1982

This will be held at the Metropole Conference Centre, Brighton, England; and will incorporate the 5th World Congress of Ultrasound in Medicine and Biology.

Over 2000 delegates are expected; many participants will also have an interest in radionuclide imaging, X rays and other investigative procedures. A large trade exhibition is being arranged as an integral part of the conference: brochure now available. Further details from: WFUMB-82 Conference Office, 4L Portman Mansions, Chiltern Street, London W1M 1LF (phone 01–486 6582).

3rd World Congress of Nuclear Medicine and Biology

Paris, August 29–September 2, 1982. Main topics: radiopharmaceuticals; radio-immunoassay; clinical applications; instrumentation; nuclear and non-nuclear investigations; radiobiology, health physics, dosimetry; economics and management. Deadline for abstracts: December 1, 1981. Information: World Federation of Nuclear Medicine and Biology, B.P.28, F-91403 Orsay, France.

World Congress on Medical Physics and Biomedical Engineering 1982

13th International Conference on Medical and Biological Engineering; 6th International Conference on Medical Physics. September 5–11, 1982, Hamburg, Federal Republic of Germany. Presidents: Prof. W. Bleifeld (Hamburg) and Prof. D. Harder (Göttingen). *Correspondence:* Hamburg Messe, Congress Organization, D-2000 Hamburg 36, Germany. P.O. Box 30 23 60.

The Neutron and its Applications

The Institute of Physics, in collaboration with AERE Harwell, is organizing an international conference in Cambridge, September 13–17, 1982, to mark the 50th anniversary of the discovery of the neutron.

The conference aims to cover all aspects of neutron science. Plenary lectures will include G. Allen on The contribution of neutron scattering to the understanding of macromolecules, J. F. Fowler on neutrons in medicine, A. M. Lane on nuclear reactions caused by neutrons, C. Llewellyn-Smith on the structure of the neutron, A. R. Mackintosh on the contribution of neutron scattering to the understanding of magnetism, N. F. Ramsay on particle properties of the neutron, and C. G. Schull on wave properties of the neutron. The conference will include a commemorative session and a public session devoted to issues of general concern. There will be exhibitions of scientific equipment, and of historical interest.

Further information from the Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.

Symposium Mammographicum 1982
(organized in co-operation with The British Institute of Radiology)

To be held on September 24–25, 1982 (1½ days) at University College, London. There will be mainly invited but some proffered papers on: (1) Various aspects of breast screening. (2) Equipment and technique of mammography. (3) Clinical, pathological and radiological features of benign breast disease. (4) Assessment of metastatic breast cancer and response to treatment. Scientific and technical exhibitions will be held.

Further information and registration forms are available from the General Secretary, The British Institute of Radiology, 36 Portland Place, London W1N 3DG. Offers of proffered papers and scientific exhibits should be addressed to Dr. C. A. Parsons, X-ray Department, Royal Marsden Hospital, Fulham Road, London SW3 6JJ.

5th South African International Radiological Congress

The 5th South African International Radiological Congress, together with a Scientific and Technical Exhibition, will be held in Johannesburg at the Carlton Hotel from October 8 to 15, 1982. The theme is "Imageology", and many of the most eminent international radiologists have been invited to participate. Honorarium lectures from overseas participants, if accepted, will be paid $250 per lecture. Further information: Dr. P. Reichman, Congress Director, PO Box 2251, Johannesburg 2000, Republic of South Africa.

7th International Congress of Radiation Research

Will be held at the International Congress Centre RAI, Amsterdam, The Netherlands, July 3–8, 1983. Information: Dr. J. J. Broerse (Secretary-general of the 7th ICRR), Radiobiological Institute TNO, PO Box 5815, 2280 HV Rijswijk, The Netherlands.

The British Journal of Radiology

FOUNDED 1896

New Series

VOLUME 54

JANUARY TO DECEMBER, 1981

The Editorial Committee consists of:

The Editors:

J. L. HAYBITTLE, M.A., PH.D. J. ROYLANCE, D.M.R.D., F.R.C.R.

The Deputy Editors:

B. T. HALE, M.B., CH.B., F.R.C.R., D.M.R.T. A. B. AYERS, M.D., D.M.R.D., F.R.C.R.
N. J. MCNALLY, B.SC., M.SC., PH.D.

and

The Associate Editors:

THELMA D. BATES, M.B., CH.B., F.R.C.R., D.C.R.A.
D. COSGROVE, M.A., B.M., B.CH., M.SC., M.R.C.P.
M. F. COTTRALL, B.A., M.SC., PH.D., F.INST.P.
J. C. W. CRAWLEY, B.SC., C.ENG., M.I.E.E.
R. DICK, M.B., B.S., M.R.A.C.R., F.R.C.R.
C. D. R. FLOWER, M.A., F.R.C.P.(C), F.R.C.R.
J. A. GLEESON, M.B., F.R.C.P., F.R.C.R., D.M.R.D.
H. GRAVELLE, B.SC., M.B., CH.B., F.R.C.P.(E), F.R.C.R., D.M.R.D.
C. H. JONES, B.SC., PH.D., F.INST.P.
D. H. KEELING, M.A., M.SC., M.B.
I. KELSEY FRY, D.M., F.R.C.P., F.R.C.R.
B. KENDALL, F.R.C.P., F.R.C.R., D.M.R.D.
H. B. MEIRE, M.B., B.S., L.C.R.P., M.R.C.S., D.M.R.D., D.OBST., R.C.O.G., F.R.C.R.
J. T. PATTON, M.R.C.S., L.R.C.P., F.R.C.R.
B. J. PERRY, B.SC., PH.D., A.R.C.S., F.INST.P.
J. R. K. SAVAGE, D.SC.
P. N. T. WELLS, D.SC., F.INST.P., F.I.E.E.

The Associate Editors Overseas are:

P. ARMSTRONG, M.B., B.S., F.R.C.R., D.M.R.D. (North America)
M. COHEN, PH.D., F.INST.P. (North America)
B. J. CREMIN, F.R.C.R., F.R.A.C.R. (South Africa)
R. FOX, D.PHIL. (Australia)
H. A. LUKE, F.R.C.R., F.R.A.C.R. (Australia)
G. P. G. SIM, M.B., CH.B., F.R.C.R., F.R.A.C.R. (New Zealand)
D. M. TAYLOR, D.SC., C.CHEM., F.R.S.C. (Continental Europe)

Managing Editor: MRS. L. F. SECRETAN, M.A.

Published by
THE BRITISH INSTITUTE OF RADIOLOGY
36 Portland Place, London W1N 3DG

© The British Institute of Radiology, 1981

INDEX TO AUTHORS

1981

Ackery, D. M. *See* Condon, B. R.; Harris, D. N. F.; Rolfe, E. B.
Ajdukiewicz, A. *See* Thompson, E. M.
Akkaraju, V. *See* Hungerford, G. D.
Allison, D. J. *See* Davies, J.; Rosenstock, J.; Timmis, J. B.
Altman, D. G. *See* Smith, T.
Alvares, R. *See* Davies, J.
Amols, H. I., Yuhas, J. M., 602
Amplatz, K. *See* Tadavarthy, S. M.
Anastasi, B., Sutherland, G. R., 679
Andersen, A. B. *See* Pettersen, E. O.
Andersen, P. E., 61
Anderson, P. *See* Dische, S.
Ansell, I. D. *See* Coggon, D. N. M.
ApSimon, H. T. *See* Khangure, M. S.
Archambeau, B. E. *See* Bennett, G. W.
Archambeau, J. O. *See* Bennett, G. W.
Archer, F. Holly *See* Holly Archer, F.
Arienti, V. *See* Bolondi, L.
Ashford, R. F. U., Maher, J., Drury, A., Pickering, D., 74
Astor, M. *See* Biaglow, T. E.
Asztély, M. *See* Nachemson, A.
Aziz, M. H. *See* Saleh, R. W.
Azzam, E. I. *See* Raaphorst, G. P.

Bacon, R. A. *See* Chivers, R. C.
Baily, B., Coe, M. A., Hearnden, T. M., 805
Baily, B. *See also* Coe, M. A.; Robertson, E.
Baird, R. N. *See* Clifford, P. C.
Bamberg, M. *See* Tamulevicius, P.
Bangert, V., Mansfield, P., Coupland, R. E., 152
Barber-Riley, P., Patel, A. S., 351
Barki, Y., Elias, H., Tovi, F., Bar-Ziv, J., 142
Barmeir, E., Mann, J. H., Marcus, R. H., 1107
Barrett, A. *See* Dobbs, H. J.
Bar-Ziv, J. *See* Barki, Y.
Bates, R. I. *See* Dewbury, K. C.
Battermann, J. J., Hart, G. A. M., Breur, K., 899
Battermann, J. J. *See also* Mijnheer, B. J.
Beachley, M. C. *See* Cho, S-R.
Beddoe, A. H. *See* Spiers, F. W.
Beek, R. v. d. *See* Veiga-Pires, J. A.
Beggs, I., 364
Beggs, I., Shaw, D. G., Brenton, D. P., Fisher, C., 416
Bell, T. K., Cranley, K., 1093
Belli, J. A. *See* Dritschilo, A.
Bennett, G. W., Dobert, R., Meltzer, J., Archambeau, B. E., Archambeau, J. O., 53
Berger, L. A., Lister, A., Lilley, A. C., 630
Biaglow, T. E., Varnes, M. E., Astor, M., Hall, E. J., 1006
Bianchi, M., Diehl-Marshall, I., 532
Bianchi, M. *See also* Diehl-Marshall, I.
Binks, C., 269
BIR Working Party on SI Units, 377
Blackledge, G., Mamtora, H., Crowther, D., Isherwood, I., 955
Bloomberg, T. J. *See* Chivers, R. C.
Bloomer, W. D. *See* Kaplan, W. D.
Bolondi, L., Casanova, P., Arienti, V., Testa, S., Gaiani, S., Labò, G., 1109
Borsa, J. *See* Raaphorst, G. P.
Boulis, Z. F., Osborne, D. R., 685
Bowley, N. B., 524
Bowley, N. B. *See also* Smith, E. E. J.
Brace, J. A., Davy, T. J., Skeggs, D. B. L., Williams, H. S., 1068
Brenton, D. P. *See* Beggs, I.,
Breur, K. *See* Battermann, J. J.
Bridge, L. R., Marshall, D. S. C., Wilson, W. P., 907
Bristol, J. B., 696
Bristol, J. B., Jones, P. A., 139
British Institute of Radiology. *See* BIR Working Party on SI Units
Broerse, J., Mijnheer, B. J., Williams, J. R., 882
Brooks, J. W. *See* Cho, S.-R.
Brown, M. J. *See* Timmis, J. B.
Bruckman, J. E. *See* Dritschilo, A.
Buchanan, R. *See* Condon, B. R.
Buchanan, W. Watson *See* Watson Buchanan, W.
Burch, P. R. J., 697
Burrows, E. H., 195
Busnardo, B. *See* Casara, D.

Calder, J. F., 819
Cameron, D. C. *See* Foster, D. R.
Campbell, W. D., Mackenzie-Crooks, D. J., 996
Caporn, N., Gilani, S., Jeans, W. D., 157
Cargill, A., Hately, W., 79
Carr, D., Walker, A., Tannahill, A. J., White, R. G., 919
Cary, P. C., Helms, C. A., Genant, H. K., 992
Casanova, P. *See* Bolondi, L.
Casara, D., Zorat, P. L., Busnardo, B., Girelli, M. E., 362
Casper, E. S. *See* Neugut, A. I.
Cassady, J. R. *See* Dritschilo, A.
Castaneda-Zuniga, W. *See* Tadavarthy, S. M.
Cattell, W. R. *See* Dixon, A. K.; Webb, J. A. W.
Causer, D. A. *See* Singh, H.
Cavallaro, A. *See* Troncone, L.
Chakera, T. M. H. *See* Khangure, M. S.
Chantler, C. *See* Saxton, H. M.
Chatterton, B. E., 1116
Chivers, R. C., Bacon, R. A., Bloomberg, T. J., 978
Chrispin, A. R. *See* Deanfield, J. E.
Cho, S-R., Henry, D. A., Beachley, M. C., Brooks, J. W., 643
Clifford, P. C., Woodcock, J. P., Baird, R. N., 348
Coakley, A. J. *See* Wells, C. P.
Coe, M. A., Baily, B., 365
Coe, M. A. *See also* Baily, B.
Coggon, D. N. M., Rose, D. H., Ansell, I. D., 418
Cohen, A., 428
Cohen, M. D., 260
Coleman, A. J. *See* Speller, R. D.
Condon, B. R., Buchanan, R., Garvie, N. W., Ackery, D. M., Fleming, J., Taylor, D., Hawkes, D., Goddard, B. A., 18
Constable, A. R., Cranage, R. W., 122, 1009
Conway, N. *See* Harris, D. N. F.
Cooke, P., Morris, P. G., 622
Cope, V. *See* Mamtora, H.
Copland, W. A. *See* Wild, S. R.
Corfield, J. R., Wells, C. P., Hall, F. M., Vernon, P., Croft, D. N., 505
Cosgrove, D. O. *See* Lowe, S. H.; Pussell, S. J.
Cotton, P. B. *See* Mason, R. R.
Coultas, P. G. *See* Hornsey, S.
Coupland, R. E. *See* Bangert, V.; Ordidge, R. J.
Cowen, A. R. *See* Hay, G. A.
Cox, T. C. S., Stevens, J. M., Kendall, B. E., 572
Cranage, R. W. *See* Constable, A. R.
Cranley, K. *See* Bell, T. K.

INDEX TO VOLUME 54

Croce, F., Montali, G., Solbiati, L., Marinoni, G., 927
Croft, D. N. *See* Corfield, J. R.
Crooks, D. J. Mackenzie *See* Campbell, W. D.
Crowther, D. *See* Blackledge, G.
Cullen, B. *See* Lunec, J.
Cullum, I. *See* Khan, O.
Cumberland, D. C., 203
Cunningham, D. A., Lavender, J. P., 110

Daintith, H. *See* Haq, A. U.
Dam, J. Van, Wambersie, A., 921
Danpure, H. J., Osnan, S., 597
Darby, S. C. *See* Wall, B. F.
Davies, J., Alvares, R., Allison, D. J., 987
Davies, P. *See* Richardson, R. E.
Davy, T. J. *See* Brace, J. A.
Day, M. J., Forster, E., 137
Day, M. J. *See also* Ross, W. M.
Deanfield, J. E., Chrispin, A. R., 856
Delaygue, C. *See* Hibbert, C. S.
Dendy, P. P. *See* Smith, F. W.
Denekamp, J. Michael, B. D., Rojas, A., Stewart, F. A., 1112
Denekamp. J. *See also* Stewart, F. A.
Dennis, N. R. *See* Paling, M. R.
Dent, D. M. *See* Schulman, A.
de Oliveira, J. B. *See* Myers, M. J.
Deschavanne, P. J., Guichard, M., Malaise, E. P., 973
Deschavanne, P. J., Malaise, E. P., Revesz, L., 361
Dewbury, K. C., Bates, R. I., 1044
Dewbury, K. C., Rao, K. S., Poll, V., 687
Dewbury, K. C. *See also* Farrant, P.
Dewhirst, D. W. *See* Shrimpton, P. C.
Dickens, C. W., 257
Dicks-Mireaux, C., Shaw, D. G., Fisher, C., 342
Diehl-Marshall, I., Bianchi, M., 530
Diehl-Marshall, I. *See also* Bianchi, M.
Dinakar, I., 701
Dische, S., Martin, W. M. C., Anderson, P., 29
Dische, S., Saunders, M. I., Stratford, M. R. L., 156
Dixon, A. K., Kelsey Fry, I., Morson, B. C., Nicholls, R. J., York Mason, A., 655
Dixon, A. K., Webb, J. A. W., Cattell, W. R., Kelsey Fry, I., 484
Dixon, A. K., Wylie, I. G., 74
Dixon-Brown, A. *See* Stedeford, B.
Dobbs, H. J., Barrett, A., Rostom, A. Y., Peckham, M. J., 878
Dobert, R. *See* Bennett, G. W.
Doll, R., 179
Doll, R. *See also* Smith, P. G.
Dolunay, H. *See* Niron, E. A.
Dossetor, R. S., Keane, B., Jeffrey, R. D., Pressburger, J., 48
Doull, F. A. M., Merrick, M. V., 1114
Down, J. D. *See* Travis, E. L.
Dritschilo, A., Bruckman, J. E., Cassady, J. R., Belli, J. A., 782
Drury, A. *See* Ashford, R. F. U.
Dubbins, P. A., O'Riordan, D. O., Melia, W. M., 307
du Boulay, G. H. *See* Wills, K.
Dubravsky, N. B., Dubrawsky, C., Jampolis, S., Mason, K., Hunter, N., Withers, H. R., 1075
Dubrawsky, C. *See* Dubravsky, N. B.
Duncan, J. G. *See* McLean, N. R.; Meek, D. R.

Edelstein, W. A., Hutchison, J. M. S., Smith, F. W., Mallard, J., Johnson, G., Redpath, T. W., 149
Edwards, J. *See* Tadavarthy, S. M.
Eichhorn, H. J., 132
Einspenner, M. *See* Raaphorst, G. P.
Ekberg, O., 496
Elias, H. *See* Barki, Y.
Ell, P. J. *See* Khan, O.
Ellert, J. *See* Thompson, E. M.
Ellwood, R. A. *See* Wesolowski, D.
Evison, G., Oliver, M., 340

Falappa, P. G. *See* Troncone, L.
Farah, J. *See* Wesolowski, D.
Farrant, P., Dewbury, K. C., Meire, H. B., 633
Farrant, P., Meire, H. B., 660
Fataar, S., Morton, P., Schulman, A., 1100
Fazio, F. *See* Gordon, I.
Federschneider, J. *See* Kaplan, W. D.
Fenech, A., Nicholls, A., Smith, F. W., 325
Fernando, D. C. J., Gopichandran, T. D., Kendrick, R. G., 72
Fernando, D. C. J. *See also* Jeans, W. D.
Finlay, D., Stockdale, H. R., Lewin, E., 870
Finlay, D. *See also* Stockdale, H. R.
Fisher, C. *See* Beggs, I.; Dicks-Mireaux, C.
Fitzgerald, M., White, D. R., White, E., Young, J., 212
Fleming, J. *See* Condon, B. R.
Formanek, A. *See* Tadavarthy, S. M.
Forster, E. *See* Day, M. J.
Foster, D. R., 817
Foster, D. R., Cameron, D. C., 995
Freeman, A. H. *See* Holly Archer, F.
Freeman, C. R. *See* Pla, M.
Friedman, M., Lawrence, B. M., Shaw, D. G., 517
Fritz-Niggli, H. *See* Michel, C.
Front, D., Israel, O., 241
Fry, I. Kelsey. *See* Kelsey Fry, I.
Fuchs, W. A. *See* Probst, P.
Fui, S. C. Ng Tang. *See* Tadros, T. G.

Gaiani, S. *See* Bolondi, L.
Gangadharan, P. *See* Sankaran, A.
Garvie, N. W. *See* Condon, B. R.; Harris, D. N. F.; Rolfe, E. B.
Genant, H. K. *See* Cary, P. C.
Geraci, J. P., 699
Ghaly, N. G. *See* Saleh, R. W.
Gilani, S. *See* Caporn, N.
Gillespie, F. C., 255
Girdwood, A. H. *See* Schulman, A.
Girelli, M. E. *See* Casara, D.
Glasser, M. *See* Howard, N.
Goddard, B. A. *See* Condon, B. R.
Godwin, T. A. *See* Neugut, A. I.
Goedemans, W. Th., 636
Gokarn, R. S. *See* Sankaran, A.
Golding, S. J. *See* Saxton, H. M.
Gopichandran, T. D. *See* Fernando, D. C. J.
Gordon, I., Helms, P., Fazio, F., 576
Gore, J. C., Hooker, G. R., 289
Grainger, R. G., Pennington, G. W., 768
Grigsby, P., Maruyama, Y., 969
Gubbay, S. S. *See* McCormick, C. C.
Gudmundsen, T. E., Kolbenstvedt, A., 422
Guichard, M. *See* Deschavanne, P. J.

Haar, G. ter. *See* Hand, J. W.
Hackett, L. P. *See* Ilett, K.

INDEX TO AUTHORS—*continued*

Haertel, M. *See* Probst, P.
Hall, C. M. *See* Stringer, D. A.
Hall, E. J., 773
Hall, E. J. *See also* Biaglow, T. E.
Hall, F. M. *See* Corfield, J. R.; Wells, C. P.
Hall, L. *See* Travis, E. L.
Hamilton S., McInerney, D., 813
Hand, J. W., ter Haar, G., 443
Handler, L., Stoch, M. B., Smyth, P. M., 953
Hansen, E. B. *See* Karle, A.
Hansen, H. *See* Holm, H. H.
Haq, A. U., Morris, A. H., Daintith, H., 1000
Harding, R. H. *See* Walker, J. K.
Harper, J. S. *See* Thompson, S. A.
Harris, D. N. F., Taylor, D. N., Ogilvie, B. C., Garvie, N. W., Watkins, J., Ackery, D. M., Conway, N., 296
Hart, G. A. M. *See* Batterman, J. J.
Hartley, D. E. *See* Khangure, M. S.
Hatazawa, J. *See* Ito, M.
Hateley, W. *See* Cargill, A.
Hawkes, D. *See* Condon, B. R.
Haworth, J. M., Watt, I., Park, W. M., Roylance, J., 932
Hay, G. A., Cowen, A. R., 24
Haycock, G. D. *See* Saxton, H. M.
Hearnden, T. M. *See* Baily, B.; Robertson, E.
Heggs, P. F. Mitchell *See* Snashall, P. D.
Helms, C. A. *See* Cary, P. C.
Helms, P. *See* Gordon, I.
Henry, D. A., *See* Cho, S-R.
Hering, E. R. *See* Mills, E. E. D.
Hibbert, C. S., Delaygue, C., McGlen, B., Porter, R. W., 905
Hildell, J., Nyman, U., Rosengren, J-E., 144
Hill, P. *See* Watt, I.
Hodgson, G. S. *See* Wigg, D. R.
Holly Archer, F., Freeman, A. H., 69
Holm, H. H., Strøyer, I., Hansen, H., Stadil, F., 665
Holmes, S. J. *See* Travis, E. L.
Hoogewoud, H. M. *See* Probst, P.
Hooker, G. R. *See* Gore, J. C.
Homer, M. J., 696
Horn, V. *See* Kolář, J. J.
Hornsey, S., 699
Hornsey, S., Myers, R., Coultas, P. G., Rogers, M. A., White, A., 1081
Hornsey, S. *See also* Lunec, J.
Horton, J. A. *See* Marano, G.
Hourihane, J. B. *See* Owens, A. P.
Howard, N., Glasser, M., 259
Howells, P. *See* Ottewell, D.
Howlett, K. A. *See* Snashall, P. D.
Huang, Miau-Ju, Liaw, Yun-Fan, Wu, Cheng-Shyong, 307
Hubmann, F-H., 250
Hungerford, G. D., Akkaraju, V., Rawe, S. E., Young, G. F., 758
Hunter, N. *See* Dubravsky, N. B.
Hutchison, J. M. S. *See* Edelstein, W. A.
Hyde, I. *See* Paling, M. R.
Hynes, M. A. *See* Reading, D. H.

Ilett, K., Hackett, L. P., Paterson, J. W., McCormick, C. C., 537
Imai, Y., Watanabe, T., Kondo, Y., Nakanishi, F., 526
Irving, J. D. *See* Mason, R. R.
Isherwood, I. *See* Blackledge, G.
Israel, O. *See* Front, D.
Ito, M., Hatazawa, J., Yamaura, H., Matsuzawa, T., 384

Jacobsen, A. B. *See* Pettersen, E. O.
Jampolis, S. *See* Dubravsky, N. B.
Jarritt, P. H. *See* Khan, O.
Jeans, W. D., Fernando, D. C. J., Maw, A. R., Leighton, B. C., 117
Jeans, W. D. *See also* Caporn, N.
Jeffrey, R. D. *See* Dossetor, R. S.
Jennings, W. A., 381
Jinks, S. *See* Millar, B. C.
Johnson, G. *See* Edelstein, W. A.
Jones, A. G. *See* Kaplan, W. D.
Jones, P. A. *See* Bristol, J. B.
Jones, P. R. M. *See* Walker, J. K.
Joplin, G. F. *See* Rosenstock, J.
Joseph, A. E. A. *See* Lowe, S. H.

Kaelin, A. C. *See* Zanelli, G. D.
Kagan, A. R. *See* Wollin, M.
Kaiser, M. C. *See* Veiga-Pires, J. A.
Kaplan, W. D., Bloomer, W. D., Jones, A. G., Federschneider, J., Knapp, R. C., 126
Karle, A., Hansen, E. B., 691, 1112
Keane, B. *See* Dossetor, R. S.
Kellershohn, C., 91
Kelsey Fry, I. *See* Dixon, A. K.; Webb, J. A. W.
Kendall, B. E., Valentine, A. R., 408
Kendall, B. E. *See also* Cox, T. C. S.
Kendall, G. M. *See* Wall, B. F.
Kendrick, R. G. *See* Fernando, D. C. J.
Kerby, I. J., 697
Keyes, S. J. *See* Snashall, P. D.
Khan, M. A. *See* Rolfe, E. B.
Khan, O., Ell, P. J., Jarritt, P. H., Cullum, I., Williams, E. S., 586
Khangure, M. S., ApSimon, H. T., Chakera, T. M. H., Hartley, D. E., 671, 1013
Kim, T. H. *See* Pla, M.
Knapp, R. C. *See* Kaplan, W. D.
Kok, G. *See* Westerman, C. G.
Kolář, J. J., Horn, V., Zídková, H., Sprindrich, J., 989
Kolbenstvedt, A., Kolmannskog, F., Lien, H. H., 423
Kolbenstvedt, A. *See also* Gudmundsen, T. E.
Kolmannskog, F. *See* Kolbenstvedt, A.
Kondo, Y. *See* Watanabe, T.
Koriech, O. M., McNaught, G. H. D., 1005
Kornelson, R. O., Young, M. E. J., 136
Koschel, K. *See* Wigg, D. R.
Kottler, R. E., Tuft, R. J., 651
Kulkarni, R. N., 875

Labò, G. *See* Bolondi, L.
Laczay, A., 364
Lamb, G. H. R., Oakley, R., 268
Laucks, S. P., McLachlan, M. S. F., 12
Lauver, J. W. *See* Vujic, I.
Lavender, J. P. *See* Cunningham, D. A.; Myers, M. J.
Laverick, M., Nias, A. H. W., 529
Lawrence, B. M. *See* Friedman, M.
Lee, R. E. J., Terry, S. I., Walker, T. M., Urquhart, A. E., 939
Leighton, B. C. *See* Jeans, W. D.
Lekias, J. S. *See* McCormick, C. C.
Leonard, J. N., Ryan, T. J., Sheldon, P. W. E., 1098
Lewin, E. *See* Finlay, D.

INDEX TO VOLUME 54

Lewis, P. D. *See* Rosenstock, J.
Liaw, Yun-Fan *See* Huang, Miau-Ju
Lien, H. H. *See* Kolbenstvedt, A.
Lilley, A. C. *See* Berger, L. A.
Lister, A. *See* Berger, L. A.
Liversage, W. E., 698
Lloyd, G. A. S., 1034
Lloyd, G. A. S. *See also* Phelps, P. D.
Loshek, D. D., Orr, J. S., Solomonidis, E., 40
Lowe, S. H., Cosgrove, D. O., Joseph, A. E. A., 754
Lunec, J., Cullen, B., Walker, H., Hornsey, S., 428

Mabey, D. *See* Thompson, E. M.
McAnulty, R. J. *See* Snashall, P. D.
McAreavey, D. *See* Meek, D. R.
McCall, I. W. *See* Park, W. M.
McCormick, C. C., Gubbay, S. S., Lekias, J. S., 140
McCormick, C. C. *See also* Ilett, K.
McDicken, W. N. *See* Wild, S. R.
Macdonald, J. S., 697
MacErlean, D. P., Owens, A. P., Hourihane, J. B., 394
McGlen, B. *See* Hibbert, C. S.
McInerney, D. *See* Hamilton, S.
McIvor, J. M. *See* Snashall, P. D.
Mackenzie-Crooks, D. J. *See* Campbell, W. D.
McLachlan, M. S. F., Wasserman, P., 488
McLachlan, M. S. F. *See also* Laucks, S. P.
McLean, N. R., McMillan, N. C., Duncan, J. G., 689
McMillan, N. C. *See* McLean, N. R.
McNaught, G. H. D. *See* Koriech, O. M.
Macpherson, P. *See* Teasdale, E.
Maher, J., Urano, M., Rice, L., Suit, H. D., 1086
Maher, J. *See also* Ashford, R. F. U.
Maisey, M. N. *See* Tadros, T. G.
Malaise, E. P. *See* Deschavanne, P. J.
Mallard, J., 831
Mallard, J. *See also* Edelstein, W. A.
Mamtora, H., Cope, V., 65
Mamtora, H. *See also* Blackledge, G.
Mann, J. H. *See* Barmeir, E.
Mansfield, P. *See* Bangert, V.; Ordidge, R. J.
Marano, G., Horton, J. A., Vazquez, A. M., 263
Marcus, R. H. *See* Barmeir, E.
Marinoni, G. *See* Croce, F.
Markowitz, R. I., Mendel, J. B., 521
Marks, I. N. *See* Schulman, A.
Marshall, D. S. C. *See* Bridge, L. R.
Martin, W. M. C. *See* Dische, S.
Maruyama, Y. *See* Grigsby, P.
Maseri, A. *See* Myers, M. J.
Mashiter, K. *See* Rosenstock, J.
Mason, A. York. *See* York Mason, A.
Mason, K. *See* Dubravsky, N. B.
Mason, R. R., Cotton, P. B., 678
Mason, R. R., Irving, J. D., 391
Matsuzawa, T. *See* Ito, M.
Maw, A. R. *See* Jeans, W. D.
Meek, D. R., Duncan, J. G., McAreavey, D., 1039
Meire, H. B. *See* Farrant, P.
Melia, W. M. *See* Dubbins, P. A.
Meltzer, J. *See* Bennett, G. W.
Mendel, J. B. *See* Markowitz, R. I.
Merrick, M. V. *See* Doull, F. A. M.; Smith, M. A.
Meurman, K. O. A., 1
Michael, B. D. *See* Denekamp, J.; Stewart, F. A.
Michel, C., Fritz-Niggli, H., 154
Mijnheer, B. J., Wieberdink, Tj., Battermann. J. J. 56
Mijnheer, B. J. *See also* Broerse, J. J.
Millar, B. C., Jinks, S., 505
Millican, P. *See* Thompson, S. A.
Mills, E. E. D., Hering, E. R., 312
Mitchell-Heggs, P. F. *See* Snashall, P. D.
Moller, J. H. *See* Tadavarthy, S. M.
Montali, G. *See* Croce, F.
Mooney, G. H., 861
Morgan, B. M. *See* Snashall, P. D.
Morgan, T. J. *See* Speller, R. D.
Morris, A. H. *See* Haq, A. U.
Morris, P. G. *See* Cooke, P.; Thomas, A.
Morson, B. C. *See* Dixon, A. K.
Morton, P. *See* Fataar, S.
Mould, R. F. *See* Robertson, E.
Mountford, P. J. *See* Webb, C. P.
Myers, M. J., Lavender, J. P., Oliveira, J. B. de, Maseri, A., 1062
Myers, R. *See* Hornsey, S.

Nachemson, A., Asztély, M., 1010
Nakanishi, F. *See* Imai, Y.
Netri, G. *See* Troncone, L.
Neugut, A. I., Casper, E. S., Godwin, T. A., Smith, J., 1002
Ng Tang Fui, S. C. *See* Tadros, T. G.
Nias, A. H. W. *See* Laverick, M.; Reading, D. H.
Nicholls, A. *See* Fenech, A.
Nicholls, R. J. *See* Dixon, A. K.
Niekerk, J. P. de V. van, 694
Niron, E. A., Ozer, H., 335
Niron, E. A., Ozer, H., Dolunay, H., 339
Norris, S. H., Watt, I., 207
Northover, J. M. A. *See* Stevens, J. M.
Nyman, U. *See* Hildell, J.

Oakley, R. *See* Lamb, G. H. R.
O'Connell, J. D., 366
O'Donoghue, E. P. N. *See* Sherwood, T.
Ogilvie, B. C. *See* Harris, D. N. F.
Oliveira, J. B. de *See* Myers, M. J.
Oliver, M. *See* Evison, G.
Olsen, K. J. *See* Pettersen, E. O.
Ordidge, R. J., Mansfield, P., Coupland, R. E., 850
O'Riordan, D. O. *See* Dubbins, P. A.
Orr, J. S. *See* Loshek, D. D.
Osborne, D. R. *See* Boulis, Z. F.
Osnan, S. *See* Danpure, H. J.
Ottewell, D., Howells, P., 430
Overgaard, J., 245
Owens, A. P. *See* MacErlean, D. P.
Ozer, H. *See* Niron, E. A.

Paling, M. R., Hyde, I., Dennis, N. R., 344, 427
Paramsothy, M., Somasundram, K., 1104
Park, W. M., Spencer, D. G., McCall, I. W., Ward, D. J., Watson Buchanan, W., Stephens, W. H., 467
Park, W. M. *See also* Haworth, J. M.
Patel, A. S. *See* Barber-Riley, P.
Paterson, J. W. *See* Ilett, K.
Peckham, M. J. *See* Dobbs, H. J.
Pennington, G. W. *See* Grainger, R. G.
Pentlow, K. S. *See* Speller, R. D.
Peters, L. L. W. *See* Thompson, E. M.
Pettersen, E. O., Olsen, K. J., Jacobsen, A. B., Andersen, A. B., 923
Phelps, P. D., Lloyd, G. A. S., 103
Pickering, D. *See* Ashford, R. F. U.

Pilling, D. W., Steiner, G. M., 562
Pitfield, J. Preston, B. J., Smith, P. G., 262
Pla, M., Podgorsak, E. B., Kim, T. H., Freeman, C. R., 412
Podgorsak, E. B. *See* Pla, M.
Poll, V. *See* Dewbury, K. C.
Porter, E. H., 1013
Porter, R. W., 1010
Porter, R. W. *See also* Hibbert, C. S.
Pressburger, J. *See* Dossetor, R. S.
Preston, B. J. *See* Pitfield, J.
Probst, P., Hoogewoud, H. M., Haertel, M., Zingg, E., Fuchs, W. A., 744
Pussell, S. J., Cosgrove, D. O., 866

Raaphorst, G. P., Azzam, E. I., Sargent, M. D., Einspenner, M., Borsa, J., 638
Rae, S. *See* Wall, B. F.
Railton, R. *See* Young, K. C.
Ramantanis, G. *See* Scavdis, S.
Ramsdale, M. L., 691
Randhawa, V. S. *See* Stewart, F. A.
Rao, K. S. *See* Dewbury, K. C.
Raphael, M. J. *See* Northover, J. M. A.
Rawe, S. E. *See* Hungerford, G. D.
Reading, D. H., Hynes, M. A., Spinks, W. S., Nias, A. H. W., 606
Reddy, E. R., 8
Redpath, T. W. *See* Edelstein, W. A.
Reenen, O.R. van, 1011
Revesz, L. *See* Deschavanne, P. J.
Reznek, R. H. *See* Webb, J. A. W.
Rice, L. *See* Maher, J.
Richards, B. A. *See* Shirley, I. M.
Richardson, R. E., Davies, P., 820
Robertson, E., Trapnell, D. H., Mould, R. F., Baily, B., Hearnden, T. M., 944
Robinson, P. J., 538
Robson, A. M., 632
Roebuck, E. J., 696
Rogers, M. A. *See* Hornsey, S.
Rojas, A. *See* Denekamp, J.
Rolfe, E. B., 694
Rolfe, E. B., Garvie, N. W., Khan, M. A., Ackery, D. M., 762
Rose, D. H. *See* Coggon, D. N. M.
Rosengren, J-E. *See* Hildell, J.
Rosenstock, J., Allison, D. J., Joplin, G. F., Lewis, P. D., Mashiter, K., Welbourn, R. B., White, M. C., 912.
Ross, W. M., Day, M. J., 819
Rostom, A. Y. *See* Dobbs, H. J.
Rothenberg, L. N. *See* Speller, R. D.
Roylance, J. *See* Haworth, J. M.
Russell, J. G. B., 701
Ryan, T. J. *See* Leonard, J. N.

Saleh, R. W., Ghaly, N. G., Aziz, M. H., 1102
Sanerkin, N. G., Watt, I., 1027
Sankaran, A., Gokarn, R. S., Gangadharan, P., 328
Sargent, M. D. *See* Raaphorst, G. P.
Saunders, J. H. *See* Smith, E. E. J.
Saunders, M. I. *See* Dische, S.
Sausman, C. *See* Whitehouse, G. H.
Savage, W. D., 695
Saxton, H. M., Golding, S. J., Chantler, C., Haycock, G. D., 555
Scavdis, S., Tritakis, G., Ramantanis, G., 146
Scherer, E. *See* Tamulevicius, P.
Schulman, A., Marks, I. N., Dent, D. M., Girdwood, A. H., 915
Schulman, A. *See also* Fataar, S.
Schwab, R. E. *See* Wesolowski, D.
Shaw, D. G., 819
Shaw, D. G. *See also* Beggs, I.; Dicks-Mireaux, C.; Friedman, M.
Sheldon, P. W. E. *See* Leonard, J. N.
Sherwood, T., O'Donoghue, E. P. N., 15
Shirley, I. M., Richards, B. A., Ward, R. H. T., 815
Shope, T. B. *See* Speller, R. D.
Showalter, C. K. *See* Speller, R. D.
Shrimpton, P. C., Dewhirst, D. W., 157, 820
Singchoovong, L. *See* Vaeusorn, N.
Singh, H., Causer, D. A., 966
Skeggs, D. B. L. *See* Brace, J. A.; Davy, T. J.
Slack, W. W. *See* Stevens, J. M.
Smith, C. B., 820
Smith, E. E. J., Saunders, J. H., Bowley, N., 266
Smith, F. W. *See* Edelstein, W. A.; Fenech, A.
Smith, F. W., Dendy, P. P., 398, 1115
Smith, J. *See* Neugut, A. I.
Smith, M. A., Merrick, M. V., Storjohann, V. F., Wong, A. J., 808
Smith, P. G., Doll, R., 187
Smith, P. G. *See also* Pitfield, J.
Smith, T., Veall, N., Altman, D. G., 961
Smyth, P. M. *See* Handler, L.
Snashall, P. D., Keyes, S. J., Morgan, B. M., McAnulty, R. J., Mitchell-Heggs, P. F., McIvor, J. M., Howlett, K. A., 277
Solbiati, L. *See* Croce, F.
Solomonidis, E. *See* Loshek, D. D.
Somasundram, K. *See* Paramsothy, M.
Speller, R. D., White, D. R., Showalter, C. K., Rothenberg, L. N., Pentlow, K. S., Morgan, T. J., Shope, T. B., 1053
Speller, R. D., White, D. R., Veerappan, R., Coleman, A. J., Waller, P. E., 232
Speller, R. D. *See also* White, D. R.
Spencer, D. G. *See* Park, W. M.
Spiers, F. W., Beddoe, A. H., Whitwell, J. R., 500
Spinks, W. S. *See* Reading, D. H.
Sprindrich, J. *See* Kolář, J. J.
Stadil, F. *See* Holm, H. H.
Stedeford, B., Dixon-Brown, A., 639
Steiner, G. M. *See* Pilling, D. W.
Stephens, W. H. *See* Park, W. M.
Stevens, J. M., Northover, J. M. A., Raphael, M. J., Slack, W. W., 909
Stevens, J. M. *See also* Cox, T. C. S.
Stewart, F. A., Randhawa, V. S., Michael, B. D., Denekamp, J., 799
Stewart, F. A. *See also* Denekamp, J.
Stoch, M. B. *See* Handler, L.
Stockdale, H. R., Finlay, D., 269, 539, 1116
Stockdale, H. R. *See also* Finlay, D.
Stoker, D. J., 1112
Storjohann, V. F. *See* Smith, M. A.
Stratford, M. R. L. *See* Dische, S.
Streffer, C. *See* Tamulevicius, P.
Stringer, D. A., Hall, C. M., 473
Strøyer, I. *See* Holm, H. H.
Suit, H. D. *See* Maher, J.; Walker, A. M.
Sundaram, A., 365
Sutherland, G. R. *See* Anastasi, B.

Tadavarthy, S. M., Formanek, A., Castaneda-Zuniga, W., Moller, J. H., Edwards, J., Amplatz, K., 736

INDEX TO VOLUME 54

Tadros, T. G., Maisey, M. N., Ng Tang Fui, S. C., Turner, P. C., 626
Tamulevicius, P., Bamberg, M., Scherer, E., Streffer, C., 318
Tannahill, A. J. *See* Carr, D.
Taylor, D. N. *See* Condon, B. R.; Harris, D. N. F.
Taylor, P. M. *See* White, D. R.
Teasdale, E., Macpherson, P., Teasdale, G., 566
Teasdale, G. *See* Teasdale, E.
Teather, D. *See* Wills, K.
ter Haar, G. *See* Hand, J. W.
Terry, S. I. *See* Lee, R. E. J.
Testa, S. *See* Bolondi, L.
Thomas, A., Morris, P. G., 615
Thompson, E. M., Ellert, J., Peters, L. L. W., Ajdukiewicz, A., Mabey, D., 518
Thompson, S. A., Harper, J. S., Millican, P., 682
Timmis, J. B., Brown, M. J., Allison, D. J., 420
Tittel, P. W., Winkler, C. F., 68
Tonge, K. A., 695
Tovi, F. *See* Barki, Y.
Trapnell, D. H. *See* Robertson, E.
Travis, E. L., Down, J. D., Hall, L., Vojnovic, B., Holmes, S. J., 50
Tritakis, G. *See* Scavdis, S.
Troncone, L., Falappa, P. G., Cavallaro, A., Netri, G., 353
Tuft, R. J. *See* Kottler, R. E.
Turner, P. C. *See* Tadros, T. G.

Urano, M., 534
Urano, M. *See also* Maher, J.
Urquhart, A. E. *See* Lee, R. E. J.

Vaeusorn, N., Viranuvatti, J., Singchoovong, L., 425
Valentine, A. R. *See* Kendall, B. E.
Van Dam, J. *See* Dam, J. Van
van Niekerk, J. P. de V. *See* Niekerk, J. P. de V. van
van Reenen, O. R. *See* Reenen, O. R. van
Varnes, M. E. *See* Biaglow, T. E.
Vazquez, A. M. *See* Marano, G.
Veall, N. *See* Smith, T.
Veerappan, R. *See* Speller, R. D.
Veiga-Pires, J. A., Beek, R. v. d., Kaiser, M. C., 269, 437
Vernon, P. *See* Corfield, J. R.
Viranuvatti, J. *See* Vaeusorn, N.
Vojnovic, B. *See* Travis, E. L.
Vujic, I., Lauver, J. W., 492

Walker, A. *See* Carr, D.
Walker, A. M., Suit, H. D., 1012
Walker, H. *See* Lunec, J.
Walker, J. K., Jones, P. R. M., Harding, R. H., 731
Walker, T. M. *See* Lee, R. E. J.
Wall, B. F., Rae, S., Darby, S. C., Kendall, G. M., 719
Waller, P. E. *See* Speller, R. D.
Wallers, K. J., 683
Wambersie, A. *See* Dam, J. Van
Ward, D. J. *See* Park, W. M.
Ward, R. H. T. *See* Shirley, I. M.
Wasserman, P. *See* McLachlan, M. S. F.
Watanabe, T. *See* Imai, Y.
Watkins, J. *See* Harris, D. N. F.
Watson Buchanan, W. *See* Park, W. M.
Watt, I., Hill, P., 592
Watt, I. *See also* Haworth, J. M.; Norris, S. H.; Sanerkin, N. G.
Webb, J. A. W., Reznek, R. H., Cattell, W. R., Kelsey Fry, I., 479
Webb, J. A. W. *See also* Dixon, A. K.
Webb, S., 673
Welbourn, R. B. *See* Rosenstock, J.
Wells, C. P., Hall, F. M., Mountford, P. J., Coakley, A. J., 1009
Wells, C. P. *See also* Corfield, J. R.
Wesolowski, D., Ellwood, R. A., Farah, J., Schwab, R. E., 982
Westerman, C. F., Kok, G., 359
White, A. *See* Hornsey, S.
White, D. R., Speller, R. D., Taylor, P. M., 221
White, D. R. *See also* Fitzgerald, M.; Speller, R. D.
White, E. *See* Fitzgerald, M.
White, M. C. *See* Rosenstock, J.
White, R. G. *See* Carr, D.
Whitehouse, G. H., Sausman, C., 429
Whitwell, J. R. *See* Spiers, F. W.
Wieberdink, Tj. *See* Mijnheer, B. J.
Wigg, D. R., Koschel, K., Hodgson, G. S., 787
Wild, S. R., Copland, W. A., McDicken, W. N., 356
Wild, S. R., McDicken, W. N., 821
Williams, E. S. *See* Khan, O.
Williams, H. S. *See* Brace, J. A.
Williams, J. R. *See* Broerse, J.
Wills, K., du Boulay, G. H., Teather, D., 948
Wilson, W. P. *See* Bridge, L. R.
Winkler, C. F. *See* Tittel, P. W.
Withers, H. R. *See* Dubravsky, N. B.
Wollin, M., Kagan, A. R., 36, 698
Wong, A. J. *See* Smith, M. A.
Woodcock, J. P. *See* Clifford, P. C.
Wu, Cheng-Shyong *See* Huang, Miau-Ju
Wylie, I. G. *See* Dixon, A. K.

Yamura, H. *See* Ito, M.
York Mason, A. *See* Dixon, A. K.
Young, G. F. *See* Hungerford, G. D.
Young, J. *See* Fitzgerald, M.
Young, K. C., Railton, R., 1091
Young, M. E. J. *See* Kornelson, R. O.
Yuhas, J. M. *See* Amols, H. I.

Zanelli, G. D., Kaelin, A. C., 403
Zatz, L. M., 695
Zingg, E. *See* Probst, P.
Zidkovà, H. *See* Kolář, J. J.
Zorat, P. L. *See* Casara, D.

INDEX TO SUBJECTS

1981

RADIODIAGNOSIS

Bones and Joints

(excluding skull)

Acetabulum excavatum in adult Down's syndrome (Case report), 340
Achondrogenesis type II in twins (Case report), 61
Assessment of progression of secondary bone lesions using serial radionuclide imaging, 18
Appraisal of use of diagnostic ultrasound to quantify lumbar spinal cord, 870
Atlanto-occipital and atlanto-axial dislocations with spinal cord compression in Down's syndrome, 758
Calcification of the posterior longitudinal ligament of the spine (Correspondence), 701
Cementifying fibroma of tibia (Case report), 989
Detection of spinal pseudarthrosis in ankylosing spondylitis, 467
Diaphyseal osteosarcoma, 932
Enchondromata with annular calcification in association with fibrous dysplasia, 1027
Histoplasma duboisii infection of bone (Case report), 518
Isolated dislocation of the pisiform (Correspondence), 364, 365
Isotope bone imaging in suspected scaphoid trauma, 762
Juvenile hyaline fibromatosis, 473
Léri's pleonosteosis (Case report), 517; (Correspondence), 819
Less common stress fractures in the foot, 1
Measurement of the lumbar spinal canal by diagnostic ultrasound (Technical note), 905; (Correspondence), 269, 430, 437, 539, 1010, 1116
Media for single contrast knee arthrography (Correspondence), 366
Metastatic disease to the carpus (Case report), 992
A "new line" in radiology (Moloney's line) (Correspondence), 691, 1112
Osteoblastic metastases in renal cell carcinoma (Case report), 1002
Osteopathia striata with sclerosis and thickening of the skull (Case report), 344, 427
Radionuclide uptake during the evolution of experimental acute osteomyelitis, 207
Recognition of the superscan in prostatic bone scintigraphy, 122
Unusual case of neurofibromatosis: cystic bone lesions and coarction of the aortic arch (Case report), 416
Upward dislocation of the first rib: a rare cause of nerve entrapment producing brachialgia (Case report), 140

Neuroradiology

(including skull)

Age-related brain atrophy and mental deterioration – CT study, 384
Cerebral nocardiosis in renal transplant patient (Case report), 1107
Clinical relevance of radiological abnormalities of the craniovertebral junction, 195
Computed tomography in diabetes insipidus: posterior empty sella (Case report), 263
CT brain scans: developmental study following gross undernutrition during infancy, 953
CT scan appearances in patients with lipoid proteinosis (Case report), 1098
Headache following various techniques with metrizamide myelography (Correspondence), 694
Hippel-Lindau syndrome in identical twins (Case report), 982
Initial findings in computer-aided diagnosis of cerebral tumours using CT scan results, 948
Myelographic study of the obstructed spinal theca with water soluble contrast medium (Technical note), 408
Osteopathia striata with sclerosis and thickening of the skull (Case report), 344, 427
Reliability of radiology in detecting prolactin-secreting pituitary microadenomas, 566
Unusual ophthalmic metastasis from a bronchial carcinoma (Case report), 146
Vascular anatomy in the suboccipital region and lateral cervical puncture, 572

Cardiovascular System

Amipaque in coronary angiography and left ventriculography, 203
Aneurysm of the splenic artery visualised by dynamic ultrasonography (Case report), 1109
The anomalous inferior vena cava (Case report), 423
Blood flow rate determination using computed tomography (Correspondence), 695
Comparison of protocols in measurement of left ventricular ejection fraction in gated blood pool scintigraphy (Technical note), 1091
Coronary collateral response and myocardial function, 731
Effect of absorption of photons by breast tissue in myocardial imaging, 966
Fate of valves of autogenous vein grafts (Case report), 348
Hypothenar hammer syndrome (Case report), 995
Intracardiac foreign body diagnosed non-invasively and removed non-surgically (Case report), 987
Left ventricular segmental wall motion – comparison between equilibrium radionuclide angiography and contrast angiography, 296
Radiographic detection of acute pulmonary oedema—comparison of radiographic appearances, densitometry and lung water in dogs, 277
Therapeutic embolization of phaeochromocytoma (Case report), 420
Three types of criss-cross heart, 736
Ultrasound features of tumour thrombus in IVC in retroperitoneal tumours, 866
Unusual case of neurofibromatosis: cystic bone lesions and coarctation of aortic arch (Case report), 416

Respiratory Tract

Chest radiograph in leptospirosis in Jamaica, 939
Chronic recurrent pleural effusion in adult histiocytosis-X (Case report), 68
Clinical applications of radionuclide lung scanning in infants and children, 576
Iatrogenic (self-induced) wet beri-beri, 1103
Intermittent cyanotic attacks in an infant—unusual presentation of congenital anterior diaphragmatic (Morgagni) hernia (Case report), 260

INDEX TO VOLUME 54

Inversion of right hemidiaphragm on ultrasound, 754
Investigation of chest disease in children by high kV fitted beam radiography, 856
Krypton 81m ventilation scanning in chronic obstructive airways disease, 110
Occult pneumothorax (Correspondence), 428
Pulmonary metastases from differentiated thyroid carcinoma detected by radionuclide imaging (Short communication), 362
Pulmonary opacities in pseudoxanthoma elasticum: report of two cases (Case report), 65
Radiation pneumonitis in a patient exposed to asbestos (Case report), 74
Radiographic detection of acute pulmonary oedema. Comparison of radiographic appearances, densitometry and lung water in dogs, 277
Radionuclide section scanning of the lungs in pulmonary embolism, 586
Recurrent non-surgical pneumoperitoneum due to spontaneous pneumothorax (Case report), 1100
Round (helical) atelectasis, 643
Unusual ophthalmic metastasis from a bronchial carcinoma (Case report), 146

Digestive Tract
Antenatal diagnosis of duodenal atresia (Case report), 633
Arteriography of Castleman tumour of the mesentery (Case report), 422
Benign greater curve gastric ulcer: the "sump-ulcer", 651
Colonic polyps in an infant following necrotising enterocolitis (Case report), 342
Deceptive duodenal deformity (Correspondence), 364
Duodenal ulcers causing obstructive jaundice and a mucocele of the gall bladder (Case report), 72
Fibrovascular polyp of the oesophagus (Case report), 142
Giant diverticulum arising from the transverse colon of a patient with diverticulosis (Case report), 683
Importance of radiological monitoring after oesophageal intubation (Case report), 996
Large bowel lymphoma complicating renal transplantation (Case report), 418
Localization of bleeding small bowel lesions for conservative re-section (Case report), 909
Lymphoma of the colon detected by CT (Case report), 144
Non-fatal intravasation of barium during barium enema (Case report), 69
Pneumatosis intestinalis in the small bowel of an adult—radiological sign of serious post-operative complication (Case report), 266
Pre-operative CT of carcinoma of the rectum, 655
Preparation for barium enema (Correspondence), 701
Pseudo tumours of the colon due to adhesions (Case report), 685
Radiology of Meconium Ileus Equivalent, 562
Radiology of the colon (BIR Proceedings), 1120
Recurrent gall-stone ileus (Case report), 1000
Recurrent non-surgical pneumoperitoneum due to spontaneous pneumothorax (Case report), 1100

Liver and Biliary Tract, Spleen, Pancreas
Biliary sludge—ultrasonic appearance simulating neoplasm (Case report), 679
Caroli's Disease: diagnosis with non-invasive methods (Case report), 526
Combined duodenoscopic and transhepatic approach to stenosis of the papilla of Vater (Case report), 678
Comparative trial of 3 oral cholecystographic contrast media (Short communication), 79
Comparison of intravenous radionuclide cholescintigraphy and ERCP in diagnosis of intrahepatic gall stones, 302
Duodenal ulcers causing obstructive jaundice and a mucocele of the gall bladder (Case report), 72
Recurrent gall-stone ileus (Case report), 1000
Resolution of multiple hepatic abscesses after percutaneous transhepatic biliary drainage, 391
Severe complications from partial splenic embolization in patients with liver failure, 492
^{99}Tc^{m} diethyl-IDA hepatobiliary scintigraphy in the preoperative diagnosis of choledochal cyst (Case report), 1104
Triple gall bladder (Case report), 817
Ultrasonography in acute cholecystitis, 927
Ultrasound appearances of liver hydatid disease, 335
Ultrasound in hepatoma—can specific diagnosis be made? 307, (Correspondence), 819

Urinary Tract
Aging and simple cysts of the kidney, 12
Bilateral renal cell carcinoma in three members of one family, 8
Calcified renal mass: chondrosarcoma of kidney (Case report), 262
Cerebral nocardiosis in renal transplant patients (Case report), 1107
Changes in sizes and distensibility of aging kidney, 488
CT vs angiography in staging of malignant renal neoplasm, 744
Diagnostic puncture in renal cystic dysplasia (multicystic kidney) evidence of aetiology of cysts, 555
Effect of DDAVP on intravenous urography, 484
Hippel-Lindau syndrome in identical twins (Case report), 982
^{111}In labelled platelets in diagnosis of renal transplant rejection, 325
Large bowel lymphoma complicating renal transplantation (Case report), 418
Lymphograms in prostatic carcinoma: false-positive and false-negative assessments in radiology, 15
Osteoblastic metastases in renal cell carcinoma (Case report), 1002
Post-biopsy haematuria successfully treated by selective transcatheter epinephrine injection (Case report), 425
Recognition of the superscan in prostatic bone scintigraphy, 122
Renal function after high dose urography in patients with renal failure, 479
Renal opacification during intravenous urography (the nephrogram in cortical necrosis) (Case report), 524
Ultrasonic demonstration of renal artery thrombosis (Case report), 351

Haemopoietic, Lymphatic, Reticulo-endothelial System

Lymphograms in prostatic carcinoma: false-positive and false-negative assessments in radiology, 15
Lymphography in post-vagotomy chylous ascites, (Case report), 915
Mediastinal lymphoscintigraphy in ovarian cancer using intraperitoneal autologous ^{99}Tc^{m} labelled erythrocytes, 126
Retroperitoneal angiomatous lymphoid hamartoma demonstrated by ultrasound (Case report), 813
Retropharyngeal bleeding in haemophilia (Case report), 521
Role of abdominal CT in lymphoma following treatment, 955

Reproductive System

Contrast media for hysterosalpingography (Correspondence), 157, 429
The Dalkon Shield (Correspondence), 695
Mediastinal lymphoscintigraphy in ovarian cancer using intraperitoneal autologous ^{99}Tc^{m}-labelled erythrocytes, 126
Second primary neoplasm in dysgerminoma patient (Case report), 1005
Ultrasound diagnosis of hydatidiform mole and coexistent fetus associated with elevated maternal serum alpha feto protein (Case report), 268
Ultrasound diagnosis of hydrops fetalis due to fetal tachycardia (Case report), 815
Ultrasound measurement of fetal limb lengths, 660

Endocrine System

CT in diabetes insipidus: posterior empty sella (Case report), 263
CT in localization of aldosterone-secreting adrenal adenomas, 1039
Diagnosis by CT of parathyroid adenoma presenting as acute pancreatitis (Case report), 689
Iodine concentration in benign and malignant thyroid nodules measured by X-ray fluorescence, 626
Reliability of radiology in detecting prolactin-secreting pituitary microadenomas, 566
Therapeutic adrenal venous infarction in ACTH dependent Cushing's syndrome (Case report), 912

Ear, nose, throat, mouth, eyes

Lacrimal gland tumours: CT and radiography, 1034
Longitudinal study of growth of nasopharynx and its contents in normal children, 117
Radiology of carcinoma of the ear, 103
Retropharyngeal bleeding in haemophilia (Case report), 521

Breast and Soft Tissues

Herniographic appearances of direct inguinal hernias in adults, 496
Juvenile hyaline fibromatosis, 473
Mammographic practice and dosimetry in Britain, 212
Symposium Mammographicum 80 (Proceedings), 159
Transgression of localizing wire into pleural cavity prior to mammography (Case report), 139; (Correspondence), 696
Unusual case of subcutaneous emphysema (Case report), 682

Paediatrics

Antenatal diagnosis of duodenal atresia (Case report), 633
Clinical applications of radionuclide lung scanning in infants and children, 576
Colonic polyps in an infant following necrotizing enterocolitis (Case report), 342
Intermittent cyanotic attacks in an infant—congenital anterior diaphragmatic (Morgagni) hernia (Case report), 260
Investigation of chest disease in children by high kV filtered beam radiography, 856
Pre-natal ultrasound demonstration of lymphangiectasia in the mesentery of the small bowel, (Case report), 687
Value of transfontanellar ultrasound in infants, 1044

Contrast Media and Other Drugs

Amipaque in coronary angiography and left ventriculography, 203
Comparative trial of three oral cholecystographic contrast media (Short communication), 79
Contrast media for hysterosalpingography (Correspondence), 157, 429
Effect of sodium/meglumine ioxaglate (Hexabrix) on thyroid function, 768
Excretion of metrizamide in milk (Correspondence), 537
Headache following metrizamide myelography (Correspondence), 694
Media for single-contrast knee arthrography (Correspondence), 366
Non-fatal intravasation of barium during barium enema (Case report), 69
Synergism of X-irradiation and radiographic contrast medium (Short communication), 919

Apparatus and Technical Aspects

Angiography assisted by new videostore system (Technical note), 48
Assessment of intravenous urogram using 100mm and conventional films, 944
Catheter system for delivery of tissue glues (bucrylate) for visceral embolization (Technical note), 671, 1013
Method of measuring radio-opacity of catheters, 289
Physical assessment of imaging performance of panel-type X-ray image intensifier, 24
Radiographic systems: what is best? (BIR Proceedings), 822
Silverless X-ray imaging (BIR Proceedings), 172

Organization and Statistics

Survey of 29 EMI CT machines in Britain, 232

Computerized Axial Tomography

(head)

Age-related brain atrophy and mental deterioration—a CT study, 384
CT scan appearances in patient with lipoid proteinosis (Case report), 1098

INDEX TO VOLUME 54

Initial findings in computer-aided diagnosis of cerebral tumours using CT scan results, 948
Lacrimal gland tumours: role of CT and conventional radiology, 1034

Computerized Axial Tomography
(whole body)

Blood flow rate determination using CT (Correspondence), 695
CT in localization of aldosterone-secreting adrenal adenomas, 1039
CT vs. angiography in staging of malignant renal neoplasms, 744
Diagnosis by CT of parathyroid adenoma presenting as acute pancreatitis (Case report), 689
Lymphoma of the colon detected by CT (Case report), 144
Pre-operative CT of carcinoma of the rectum, 655
Rib artefact in CT (Short communication), 78
Role of abdominal CT in lymphoma following treatment, 955

Computerized Axial Tomography
(apparatus and technical aspects)

Evaluating performance characteristics in CT, 221
Evaluation of CT systems from 10 manufacturers, 1053
Survey of 29 EMI CT machines in Britain, 232
X-ray tube lifetime and image quality in CT (Correspondence), 820
X-ray tube lifetimes with the Leeds EMI brain scanner (Correspondence), 157

RADIOTHERAPY
Results and Clinical Aspects

Brachytherapy build-up factors (Scientific note), 136
Choosing between two formulations of a dose/cure function (Correspondence), 1012, 1013
Combined radiotherapy & chemotherapy—can radiobiology help? (BIR Proceedings), 707
Different fractionation schemes tested by histological examination of autopsy specimens from lung cancer patients, 132
Dose-effect relations of tumour control and complication rate after fast neutron therapy for pelvic tumours, 899
Effects of dose fractionation after irradiation with neutrons produced by 600 MeV protons (Short communication), 532
Excretion of metrizamide in milk (Correspondence), 537
Improved therapeutic technique for prophylaxis of the central nervous system in patients with acute lymphoblastic leukaemia (Technical note), 412
Induced radioactivity in patients from betatron irradiation (Technical note), 53
Induction of micronuclei by irradiation with neutrons produced from 600 MeV protons (Short communication), 530
Induction of spinal cord paralysis by negative pi-mesons, 602
In vivo dosimetry in the pelvis during fast neutron therapy (Technical note), 56
^{131}I ablation therapy for a patient on maintenance haemodialysis (Case report), 259
Management of soft tissue tumours by limited surgery combined with tumour bed irradiation using brachytherapy and supplementary teletherapy, 312
Misonidazole as a radiosensitizer in radiotherapy of glioblastomas and oesophageal cancer pharmacokinetic and clinical studies, 318
OER and RBE variation between p(75)-Be and d(50)-Be neutron beams (Short communication), 921
Osteoblastic metastases in renal cell carcinoma (Case report), 1002
Para-aortic nodes in carcinoma of the cervix (Correspondence), 697
Pulmonary metastases from differentiated thyroid carcinoma detected by radionuclides (Short communication), 362
Radiation myelopathy in patients treated for carcinoma of bronchus using a six fraction regime, 29
Relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract, 36; (Correspondence), 698, 699
Second primary neoplasm in a dysgerminoma patient (Case report), 1005
Symposium in honour of Dr Frank Ellis (BIR proceedings), 168
Tolerance of brain to multiple courses of radiation therapy. I, 782
Tolerance of mature human central nervous system to photon irradiation, 787
Use of thiol compounds to protect normal tissues in radiotherapy (Correspondence), 428, 1112
Vocal cord paralysis after treatment of thyrotoxicosis with radioiodine (Case report), 632
Whole-body irradiation (BIR proceedings), 370

Apparatus and Technical Aspects

Conformation therapy at Royal Free Hospital-tracking Co project, 1068
European protocol for neutron dosimetry for external beam therapy, 882
Gold grain dosimetry (Correspondence), 269
Improved radiotherapeutic technique for prophylaxis of central nervous system in patients with acute lymphoblastic leukaemia (Technical note), 412
Management of soft tissue tumours by limited surgery combined with tumour bed irradiation using brachytherapy and supplementary teletherapy, 312
Measurement of chest-wall thickness using simulator (Technical note), 359
Mullard 4MV linear accelerator at Newcastle upon Tyne (Correspondence), 819
Negative pion depth-dose profile examined by means of HeLa cell-survival curves, 606
New modalities in cancer treatment: heavy charged particles, 773
New rectal marker for treatment planning (Correspondence), 365
New technique for radiation shielding in superficial X-ray therapy (Technical note), 805
Personalized fixation using vacuum consolidation technique (Technical note), 257
Portable transfer digital dosemeter for beam output measurements with X and gamma rays, electrons and neutrons, 328
Radiation doses in neutron therapy (Correspondence), 699

Applied to Other Aspects of Radiology (Ultrasonics, Thermography etc.)

Accuracy of dimensional measurement in ultrasonic real-time scanning (Technical note), 978
Evaluation of count rate losses due to dead time in static and mobile gamma camera data analysis systems (Technical note), 1093
Heating techniques in hyperthermia (Review article), 443
Hybrid real time/B scan ultrasonic system—implications for clinical practice based on a 2-year experience (Technical note), 356; (Correspondence), 820,821
Water bath for thyroid scanning with ultrasound (Technical note), 630

RADIOBIOLOGY

Brachytherapy build-up factors (Scientific note), 136
Choosing between two formulations of a dose/cure function (Correspondence), 1012
Combined radiotherapy & chemotherapy—can radiobiology help? (BIR Proceedings), 707
Different fractionation schemes tested by histological examination of autopsy specimens from lung cancer patients, 132
Dose-effect relations of tumour control and complication rate after fast neutron therapy for pelvic tumours, 899
Effect of dexamethasone on radiation survival response and misonidazole-induced hypoxic-cell cytotoxicity in Chinese hamster cells V-79-753B *in vitro*, 505
Effect of X irradiation on rectum of the rat, 250
Effects of dose fractionation after irradiation with neutrons from 600 MeV protons (Short communication), 532
Factors affecting breathing rate of mice as used for studies of radiation damage to lungs (Technical note), 50
Induction of micronuclei by irradiation with neutrons from 600 MeV protons (Short communication), 530
Long-term effects of pulmonary damage on lung weight, compliance, hydroxyproline content, and metastasis formation in mice, 1075
Mechanisms of misonidazole-linked cytotoxicity and altered radiation response—role of cellular thiols (Short communication), 1000
Modification of oral radiation death syndrome with combined WR 2721 and misonidazole, 969
Negative pion depth-dose profile examined by HeLa cell-survival curves, 606
Neurotoxicity with desmethylmisonidazole (Correspondence), 156
OER and RBE variations between p(75)Be & d(50)Be neutron beams (Short communication), 921
Oncogenic potential of X rays and/or hyperthermia in C3H-10T$\frac{1}{2}$ cells (Correspondence), 638
Potentiation of radiation response of hypoxic mammalian cells by CHIP (Short communication), 529
Radiation survival of glutathione-deficient human fibroblasts in culture (Short communication), 361
Radiobiology forum on non-stochastic effects of ionizing radiations (MRC), 81
Radiobiology work-in-progress meeting (BIR Proceedings February 1981), 709
Radiobiology work-in-progress—radiosensitizers and radioprotectors (BIR Proceedings), 367
Radiosensitivity of lymphocytes separated from rat lymph nodes and human peripheral blood, (Correspondence), 923
Relationship of dose to prognosis in squamous-cell carcinoma of the aerodigestive tract, 36; (Correspondence), 698, 699
Repair during fractionated irradiation of mouse bladder, 799
Repair of sublethal & potentially lethal damage in lung cells using *in vitro* colony method, 973
Synergism of X irradiation and radiographic contrast medium (Short communication), 919
Teratogenic and radiosensitizing effects of misonidazole on mouse embryos (Short communication), 154
Thermal resistance in a spontaneous murine tumour, 1086
Turnover of proliferative cells in spinal cord after X-irradiation & relation to time-dependent repair of damage, 1081

HYPERTHERMIA

Effect of hyperthermia on hypoxic fraction in experimental mammary carcinoma *in vivo*, 245
Heating techniques in hyperthermia (Review article), 443
Hyperthermia (BIR Proceedings), 1117
Interaction of hyperthermia and radiation: radiation quality, 40
Long-term observation of mouse foot reaction after hyperthermia: hyperthermia may or may not be carcinogenic (Short communication) 534
Oncogenic potential of X-rays and/or hyperthermia in C3H-10T$\frac{1}{2}$ cells (Correspondence), 638
Thermal resistance in spontaneous murine tumour, 1086

HAZARDS AND RADIATION PROTECTION

Dosimetry and risks to patients in radiopharmaceutical investigations (BIR Proceedings), 431
Dosimetry of renal radiopharmaceuticals: bladder radioactivity and a simple aid for its estimation, 961
Effects of NMR exposure on living organisms 1. Microbial assay, 615
Effects of NMR exposure on living organisms. 2. Genetic study of human lymphocytes, 622
Inductions of spinal cord paralysis by negative pi-mesons, 602
Long-term observation of mouse foot reaction after hyperthermia—hyperthermia may or may not be carcinogenic (Short communication), 534
Mean skeletal dose factors for beta-particle emitters in human bone. 2. Surface-seeking radionuclides, 500
Monte Carlo calculations of dose distribution across plane bone marrow interface during diagnostic X-ray examinations, 875
Mortality from cancer and all causes among British radiologists, 187
Protective effect of spectacles (Technical note), 137
Radiation dose from human platelets labelled with ^{111}In (Correspondence), 1011
Radiation hazards: 25 years of collaborative research (Silvanus Thompson Lecture, 1980), 179

INDEX TO VOLUME 54

Radiation hazards (Correspondence), 697
Radiobiology forum on non-stochastic effects of ionizing radiations (MRC), 81
Radiology and risk—economist's perspective, 861
Radiosensitivity of lymphocytes separated from rat lymph nodes and human peripheral blood (Correspondence), 923
Reappraisal of genetic consequences of diagnostic radiology, 719
Synergism of X irradiation and radiographic contrast medium, (Short communication), 919
The "ten-day rule" (Correspondence), 691
Vocal cord paralysis after treatment of thyrotoxicosis with radioiodine (Case report), 632

NUCLEAR MAGNETIC RESONANCE

Effects of NMR exposure on living organisms. 1. Microbial assay, 615
Effects of NMR exposure on living organisms. 2. Genetic study of human lymphocytes, 622
Human whole-body NMR tomographic imaging: normal sections (Short communication), 149
Rapid biomedical imaging by NMR, 850
The Noes have it—do they? (Silvanus Thompson Lecture 1981), 831
Whole-body tomographic imaging by NMR (Short communication), 152

LECTURES AND ADDRESSES

The Noes have it—do they? (Silvanus Thompson Memorial Lecture 1981), 831
Positron emitting radionuclides in the study of metabolic and physiopathologic mechanisms (Mackenzie Davidson Memorial Lecture 1980), 91
Radiation hazards: 25 years of collaborative research (Silvanus Thompson Memorial Lecture 1980), 179

PROCEEDINGS OF MEETINGS

British Institute of Radiology 38th Annual Congress, 1980—addendum, 84
British Institute of Radiology 39th Annual Congress, 1981, 1014
British Institute of Radiology Annual Congress Scientific Exhibition, 1981, 825
British Institute of Radiology Symposium in honour of Dr. Frank Ellis (September 1980), 168
British Medical Ultrasound Society 12th Annual Meeting, 1980, 540
Combined radiotherapy and chemotherapy—can radiobiology help? (British Institute of Radiology, February 1981), 707
Dosimetry and risks to patients in radiopharmaceutical investigations (British Institute of Radiology, November 1980), 431
Hyperthermia (British Institute of Radiology, May 1981), 1117
Radiobiology forum on non-stochastic effects of ionizing radiations (MRC, March 1980), 81
Radiobiology work-in-progress (British Institute of Radiology, February 1981), 709
Radiographic systems: what is best? (British Institute of Radiology, March 1981), 822
Radiology of the colon (British Institute of Radiology, May 1981), 1120
Radionuclides in gastroenterology (British Institute of Radiology, February 1981), 702
Radiosensitizers and radioprotectors (British Institute of Radiology, November 1980), 367
Silverless X-ray imaging (British Institute of Radiology, October 1980), 172
Symposium Mammographicum 80, 159
Whole-body irradiation (British Institute of Radiology, November 1980) 370

AWARDS

British Institute of Radiology Awards 1981, 713

OBITUARIES

J. D. Frye, 701
Dr. F. H. Howarth, 435
Dr. H. E. Jones, 176
Prof. Ralston Paterson, 1122
Dr. F. G. Spear, 375

BOOK REVIEWS

ABC Radiodiagnostic. 3. Radiologie vasculaire, 301
Abdominal ultrasound, 276
Abdominal ultrasound in the cancer patient, 757
Advances in neurosurgery. 7. Neurovascular surgery, 121
Alimentary tract radiology, 397
Application of the dose limitation system for radioprotection, 88
Atlas of computerized emission tomography, 125
Atlas of disease and special examination of the breast, 77
Atlas of the human brain for computerized tomography, 402
Atlas of lymphography, 270
Atlas of radiologic anatomy, 7
Basic bone radiology, 860
Biology of ovarian neoplasia, 536
Bone metastases, 938
Bone tumors. Diagnosis and treatment, 275
Cahiers de radiologie. 2. Le crâne, 938
Cancer, 898
Cancer and the immune response, 35
Cancer risks by site, 904
Cardiac nuclear medicine, 301
Cardiovascular nuclear medicine. Current methodology and practice, 554
Cases in diagnostic ultrasound. 1, 670
Catalogue of spectral data for diagnostic X-rays, 87
Cellular radiobiology, 614
Cerebral aneurysms, 121
Choix d'un système informatique pour le calcul des doses en radiotherapie, 908
Clark's positioning in radiography, 177
Clinical cardiac radiology, 23
Clinical gynecologic oncology, 1074
Clinical neuro-ophthalmology, 1038
Clinical ultrasound review, 664
Clinics in diagnostic ultrasound. 4. Two-dimensional echocardiography. 5. New techniques and instrumentation, 1008
Computed tomography and cerebral infarctions, 1061
Correlative neuroradiology, 402
Correlative sectional anatomy of the head and neck, 121

Dacryocystography, 17
Diagnostic imaging of the kidney and urinary tract in children, 1043
Diagnostic radiation: a possible factor in malignancy in patients with chronic inflammatory bowel disease, and other essays, 904
Diagnostic ultrasound, 275
Dictionary of medical ethics, 1123
Differentialdiagnose seltener Lungenerkrankungen im Röntgenbild, 77
Disorders of the cervical spine, 7
Draft British Standard DD66. Leak testing for sealed radioactive sources, 637
Effects of irradiation on the small intestine of the rat, 440
Effects on populations of exposure to low levels of ionizing radiation, 898
Embryogenesis of the human skull, 553
Encyclopaedia of Medical Radiology. 5, 6. Bone tumours, 275
Endoscopic retrograde cholangiopancreatography, 483
Endoscopy and biopsy in gastroenterology, 716
Environmental health criteria. 14. Ultraviolet radiation, 972
Essential physics for radiographers, 178
Fast neutrons in the treatment of cancer, 605
Fundamental and clinical bone physiology, 767
Forensic fetal osteology, 495
Fundamental approaches to radiologic special procedures, 1090
Gastrointestinal radiology, 87
Glucagon in gastroenterology, 88
Grenz rays: an illustrated guide, 504
Guide pratique d'echographie abdominale, 276
Gynaecological radiology, 968
Handbuch der medizinischen Radiologie. 1A. Nuklearmedizin, 273
  XIII, 2. Roentgendiagnostik des Urogenitalsystems—Weibliches Genitale, 131
Health implications of nuclear power production, 1085
Heavy particle radiotherapy, 324
A history of X rays and radium, 1121
Hodgkin's Disease, 718
Illustrated guide to X-ray technics, 173
Induced disease—drugs, irradiation, occupation, 659
Influence of dose and its distribution on dose-response relationships (NCRP Report 64), 717
Information processing in medical imaging, 178
Interpreting dental radiographs, 553
Introduction to cerebral angiography, 438
Introduction to diagnostic radiology, 1097
Introduction to diagnostic ultrasound, 664
Introduzione alla medicina nucleare, 625
Investigative ultrasonology. 1, Technical advances, 631
Known effects of low-level radiation exposure, 625
Lecture notes in biomathematics, 1013
Lecture notes on clinical oncology, 881
Low back disability, 376
Lumbale Myelographie mit wasserlöslichen Kontrastmitteln, 874
Mammography (NCRP Report 66), 717
Management of persons accidentally contaminated with radionuclides (NCRP Report 65), 798
Manual of ultrasonography, 311
Manuel de techniques radiographiques du crâne, 849
Mathematics for technologists in radiology, 372
Measurement of the performance characteristic of diagnostic X-ray systems, 311
Medical physics handbooks
  6. Fundamentals of radiation dosimetry, 717
  7. Radiotherapy treatment planning, 781
  8. Nuclear particles in cancer treatment, 716
Multiple imaging procedures. 4. Urinary tract and adrenal glands, 947
The narrow lumbar canal, 270
Natural radiation environment, 3, 977
Noncoherent optical processing, 334
Nuclear Medicine Annual 1980, 249
Nuclear medicine examination review, 585
Nuclear medicine—focus on clinical diagnosis, 855
Nuclear medicine: hepatolienal, 585
Nuclear medicine physics, 306
Oncology Supplement: scientific foundations of oncology, 466
Optimization of radiotherapy, 637
Pediatric ultrasound, 276
Perceptions of risk, 372
Physics in nuclear medicine, 438
Physics of medical imaging, 178
Pitfalls in pediatric chest radiography, 177
Practical introduction to cranial CT, 849
Practice of biliary surgery, 288
Professional approach to radiology administration, 220
Progress in nuclear medicine. 6. Cardiovascular nuclear medicine, 554
Quality assurance measurements in diagnostic radiology, 306
Quality assurance of radiopharmaceuticals—guide to hospital practice, 427
Quantitative concepts and dosimetry in radiobiology, 376
1001 questions about radiologic technology, 440
Radiant energy and the eye, 334
Radiation drug interactions in the treatment of cancer, 516
Radiation oncology—rationale, technique, results, 131
Radiation protection. Ion chambers for neutron dosimetry, 1111
Radiation protection optimization, 972
Radiation quantities and units, 380
Radiation therapy technology examination review, 135
Radiographic atlas of colon disease, 88
Radiographic photography and imaging processes, 439
Radiologic science for technologists, 439
Radiology of bone disease, 650
Radiology of the colon, 177
Radiology of the colon (Golden's Diagnostic Radiology 21), 177
Radiology of haemophilic arthropathies, 274
Radiology of tuberculosis, 116
Radiology of the urinary system, 438
Radionuclide imaging artefacts, 965
Reflux nephropathy, 366
Renal adenocarcinoma, 924
Renal microvascular disease angiographic-microangiographic correlates, 654
Repères et mesures en radiodiagnostic, 440
Review of gross anatomy, 87
Review of medical terminology, 231
Das Röntgenbild, 173
Roentgenologic anatomy, 295

INDEX TO VOLUME 54

Roentgenology of lymphomas and leukemias, 881
Die Röntgenuntersuchung im Kindesalter, 220
Science in action, 202
Scintillation camera acceptance testing and performance evaluation, 855
Screening for cancer: theory, analysis and design, 274
Screening in cancer: UICC international workshop, 274
Self-assessment of current knowledge in diagnostic radiology, 177
Single photon emission computed tomography (symposium), 504
Textbook of radiology and imaging, 565
Therapeutic progress in ovarian and testicular cancer and sarcomas, 438
Therapy and prevention of infections in cancer patients, 35
Thermal characteristics of tumours, 439
Thermoluminescence dosimetry, 539
Topical reviews in radiotherapy and oncology, 516
Trattato di senologia, 491
Treatment of radioresistant cancers, 60
Ultrasonic tissue characterisation, 981
Ultrasonically guided puncture technique, 670
Ultrasound in medicine and biology, 311
Ultrasound of the pediatric abdomen and pelvis, 495
L'urographie intraveineuse, 17
Uroradiology, 821
UV-A biological effects of ultraviolet radiation, 273
La xeromammografia, 167
1980 Year book of nuclear medicine, 249

MISCELLANEOUS

Analysis of publications, 1978–80, 640
Conversion to SI units in radiology, 377
European Society for Therapeutic Radiology and Oncology, 552
Strategic marking in MCQ papers (Correspondence), 538

REVIEW ARTICLE

Heating techniques in hyperthermia, 443

Proceedings of The British Institute of Radiology. 1117
Radiobiology work-in-progress: hyperthermia: May 22, 1981.
Radiology of the colon: May 14, 1981.

Obituary: Professor Ralston Paterson 1122

Forthcoming events and notices. 1124

Book reviews

Clinical neuro-ophthalmology 1038

Diagnostic imaging of the kidney and urinary tract in children 1043

Computed tomography and cerebral infarctions 1061

Clinical gynecologic oncology 1074

Health implications of nuclear power production 1085

Fundamental approaches to radiologic special procedures 1090

Introduction to diagnostic radiology 1097

Radiation protection. Ion chambers for neutron dosimetry 1111

A history of X rays and radium 1121

Dictionary of medical ethics 1123

Treatment Simulators

British Journal of Radiology Supplement 16, 1981

This is a revised version of a working-party report which was first published in 1976 as BIR Special Report 10, and owing to heavy demand has been out of print for some time. The authors consider the place of planning simulators in modern radiotherapy and endeavour to set up guide lines for their future development, covering both specifications for the instruments and the ways in which they are used. The report also discusses the relationship between simulators and transverse axial computed tomography.

The report has been fully updated and is highly detailed, containing 31 pages, 10 figures, and 59 references covering the period 1952 to 1981. The Convenor of the Working Party was C. K. Bomford and other members were Miss L. M. Craig, F. A. Hanna, G. S. Innes, S. C. Lillicrap and the late R. L. Morgan, with G. R. Higson as DHSS Observer.

Of practical interest to all involved with developments in radiotherapy.

ISSN 0306–2120 Price £3.50

Orders to:

Publications Department, The British Institute of Radiology,
36 Portland Place, London W1N 3DG
Tel: 01-580 4189 or through your bookseller.

VOL 54 NO 648
DECEMBER 1981

The British Journal of Radiology

Contents

Page

Enchondromata with annular calcification in association with fibrous dysplasia. 1027
N. G. Sanerkin and Iain Watt

Lacrimal gland tumours: the role of CT and conventional radiology. 1034
G. A. S. Lloyd

Computed tomography in the localization of aldosterone-secreting adrenal adenomas. 1039
D. R. Meek, J. G. Duncan and D. McAreavey

The value of transfontanellar ultrasound in infants. 1044
K. C. Dewbury and R. I. Bates

An evaluation of CT systems from ten manufacturers. 1053
R. D. Speller, D. R. White, C. K. Showalter, L. N. Rothenberg, K. S. Pentlow, T. J. Morgan and T. B. Shope

A simplified method of quantitating organ uptake using a gamma camera. 1062
M. J. Myers, J. P. Lavender, J. B. de Oliveira and A. Maseri

Conformation therapy at the Royal Free Hospital. A progress report on the tracking cobalt project. 1068
J. A. Brace, T. J. Davy, D. B. L. Skeggs and H. S. Williams

Long-term effects of pulmonary damage in mice on lung weight, compliance, hydroxyproline content and formation of metastases. 1075
N. B. Dubravsky, C. Dubrawsky, S. Jampolis, K. Mason, N. Hunter and H. R. Withers

Turnover of proliferative cells in the spinal cord after X irradiation and its relation to time-dependent repair of radiation damage. 1081
Shirley Hornsey, R. Myers, P. G. Coultas, M. A. Rogers and Ann White

Thermal resistance in a spontaneous murine tumour. 1086
Jane Maher, M. Urano, L. Rice and H. D. Suit

Technical notes. 1091
- Comparison of protocols in the measurement of left ventricular ejection fraction in gated blood-pool scintigraphy.
  K. C. Young and R. Railton
- An evaluation of count rate losses due to dead time in static and mobile gamma camera data analysis systems.
  T. K. Bell and K. Cranley

Case reports. 1098
- CT scan appearances in a patient with lipoid proteinosis.
  J. N. Leonard, T. J. Ryan and P. W. E. Sheldon
- Recurrent non-surgical pneumoperitoneum due to spontaneous pneumothorax.
  S. Fataar, P. Morton and A. Schulman
- Iatrogenic (self-induced) wet beri-beri.
  R. W. Saleh, N. G. Ghaly and M. H. Aziz
- Technetium 99m-diethyl-IDA hepatobiliary scintigraphy in the pre-operative diagnosis of choledochal cyst.
  M. Paramsothy and K. Somasundram
- Cerebral nocardiosis in renal transplant patients.
  E. Barmeir, J. H. Mann and R. H. Marcus
- A case of aneurysm of the splenic artery visualized by dynamic ultrasonography.
  L. Bolondi, P. Casanova, V. Arienti, S. Testa, S. Gaiani and G. Labò

Correspondence. 1112
- Moloney's line.
  D. J. Stoker; A. Karle and E. B. Hansen
- Thiol radioprotection *in vivo*: the critical role of tissue oxygen concentration.
  J. Denekamp, B. D. Michael, A. Rojas and F. A. Stewart
- Modification of gallium 67 citrate distribution in man following the administration of iron.
  F. A. M. Doull and M. V. Merrick; F. W. Smith and P. P. Dendy
- Use of ultrasound to measure the lumbar spinal canal.
  B. E. Chatterton; H. R. Stockdale and D. Finlay

(continued on inside back cover)

Printed in Great Britain by Lund Humphries
London and Bradford
Published by THE BRITISH INSTITUTE OF RADIOLOGY
36 Portland Place, London W1N 3DG

ISSN 0007-1285
17397